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PROGRESSIVE CHANGES IN PULMONARY FUNCTION AFTER PNEUMONECTOMY: THE INFLUENCE OF THORACOPLASTY, PNEUMOTHORAX, OLEOTHORAX, AND PLASTIC SPONGE PLOMBAGE ON THE SIDE OF PNEUMONECTOMY

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THE fate of the remaining lung after pneumonectomy has been a matter of great concern to thoracic surgeons and the subject of a number of interesting and revealing physiologic studies.[1-5] As pneumonectomy is being carried out successfully for an increasing variety of diseases including tuberculosis, and as the average age of the patients operated upon decreases, establishment of optimal conditions for the preservation of function of the remaining lung becomes increasingly important.

Previous investigations of lung volume after pneumonectomy have demonstrated that a variable amount of overdistention of the remaining lung occurs, though this is not as severe in man as in the experimental animal.[1, 2, 4, 6, 7] Overdistention is generally thought to be undesirable in patients with pulmonary tuberculosis. The current thought is that a lung with a larger volume than normal doing twice its normal work is more susceptible to reactivation of disease and handles residual disease poorly.[8] Overdistention causes a variety of complaints due to displacement of the mediastinum. The worst of these is ineffective cough due to angulation of the trachea.

Both Birath and Cournand have demonstrated that intrapulmonary mixing of gases is impaired in the remaining overdistended lung.[1, 2] The great variability of the physiopathologic pattern was well shown by follow-up studies after pneumonectomy in childhood.[9, 10] Cournand suggested early that thoracoplasty might prevent the development of contralateral pulmonary distention without further impairing maximal function.[1] However, during a recent extensive

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study of cardiorespiratory function after total resection he showed that thoracoplasty on the pneumonectomy side leading to scoliosis reduces the ventilatory effectiveness of the remaining lung.[4]

Investigations of pulmonary function after pneumonectomy have provided only a partial answer to the problem of the management of the empty hemithorax for several reasons. The number of patients studied was usually small. Often it was evident that older patients, in whom emphysema of the remaining lung was found, must have had this disease prior to operation. Following resection for bronchogenic carcinoma it was frequently not clear whether progressive loss of function was due to overdistention or extension of the tumor.[3] Studies performed on one or two occasions some time after pneumonectomy did not reveal during what period after resection the changes in the remaining lung had occurred. Lastly, since the volume and function of the "good" lung alone prior to operation was never known, it has not been clear whether functional changes after pneumonectomy were due to resection of functioning lung tissue, due to progressive physiologic changes of the remaining lung, or due to a combination of both.

For an understanding of the development of functional defects of the remaining lung and for a rational approach toward establishment of ideal conditions for functional preservation of the remaining lung, a plan of investigation was made which was thought necessary for a solution to the problem of overdistention. Prior to operation a bronchospirometric method was used which permitted not only determination of oxygen uptake, ventilation, and vital capacity, but also permitted determination of residual volume, total lung capacity, and pulmonary mixing indices for the two lungs separately.[11] The state of overdistention of the remaining lung could therefore be established prior to operation. The residual volume technique was modified for this study to permit appreciation of small changes in this value.[11] To establish the time after operation when the greatest changes in the remaining lung take place, patients were studied at weekly intervals immediately after operation and at monthly intervals thereafter. To obtain an adequate long-term follow-up of all patients studied prior to operation, patients with carcinoma were excluded from the study.

METHOD

The Darling open circuit oxygen method[12] for determination of the total lung capacity was modified for this investigation, and a new bronchospirometric technique was developed for determination of differential lung volumes. These methods will be described in more detail elsewhere.[11]

Total Lung Capacity.—The final volume of gas obtained by the open circuit method depends on the exact place in the respiratory cycle at which the patient is switched from room air to oxygen breathing. This circuit change is made at the end of a quiet or forced expiration, depending on whether one desires to measure the functional residual or the true residual fractions of the lung volume. Since it is difficult to switch at the very end of forced expiration, particularly in patients who are somewhat dyspneic, the change is usually made

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at the end of a quiet respiration.[13] The correct timing is ascertained by observing the patient's respiratory movements. In a normal subject, the functional residual volume averages 1,500 cubic centimeters. If a switching error of 150 c.c. or one-fourth of a tidal breath is made, this introduces an error of 10 per cent in the calculated functional residual volume. After pneumonectomy, the functional residual volume averages 800 c.c., and not infrequently 500 c.c. or less. A similar error in estimation of the end of a quiet expiration then causes an error of 20 to 30 per cent of the calculated volume, a much larger variation in itself than the true changes in volume which may be expected to

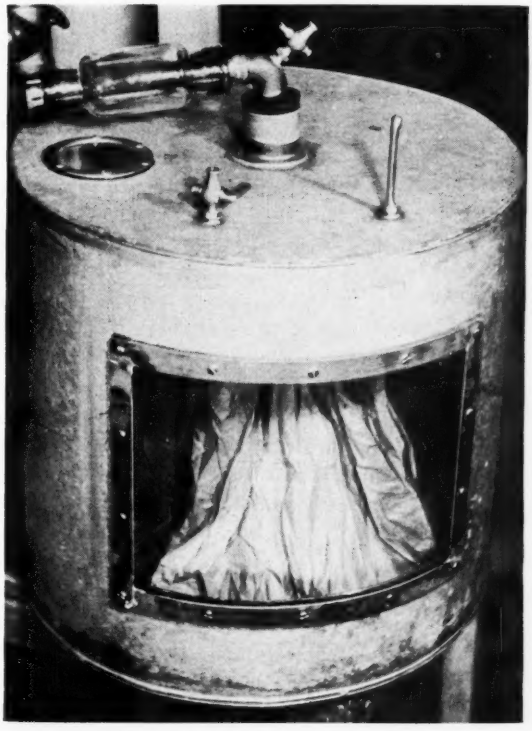

Fig. 1.—Balloon within air-tight box permitting ambient air spirometry.

take place from month to month after pneumonectomy. Furthermore, correct timing of the change from room air to oxygen is made more difficult by the more rapid respiratory rate shortly after pneumonectomy. All calculations are based on the assumption that the lungs initially contained 81 per cent nitrogen. Ordinary recording spirometry, therefore, cannot be used prior to lung volume determination, since this would change the initial composition of gas in the lungs.

Three changes were made to increase the accuracy of the method. Prior to oxygen breathing, patients inspired room air from a rubber balloon enclosed

in an airtight box and expired into the box around the balloon* (Fig. 1). The box was also connected to a recording spirometer. As the patient inspires, the pressure in the box decreases and the spirometer bell descends and, as the patient expires, the reverse takes place. Thus, although the patient breathes room air, a spirogram can still be obtained. This permits not only better observation of the breathing cycle, but any switching error can later be measured from the spirogram and added or deducted from the calculated functional residual volume (Fig. 2). Two further changes were made. An alveolar trap was used

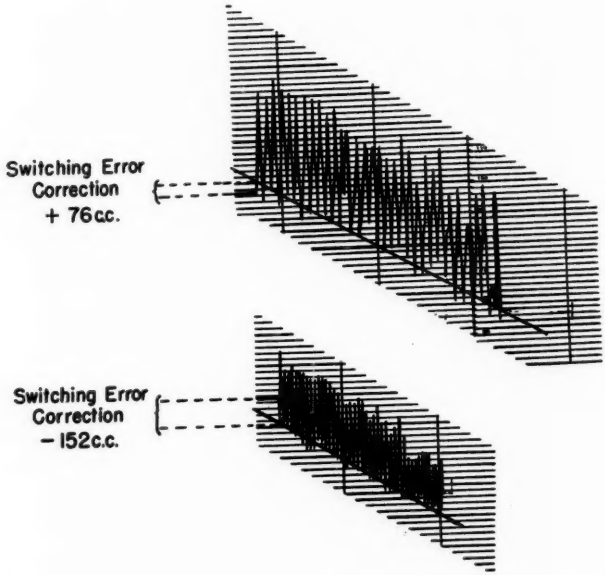

Fig. 2.—Ambient air spirograms obtained prior to oxygen breathing for determination of the functional residual capacity. The switching error can be measured from the tracing.

for collection of a terminal alveolar sample as suggested by Wright.[14] This assures collection of alveolar air even in patients who are dyspneic. Finally, an oxygen flushed Douglas bag was used instead of a Tissot spirometer for collection of expired gas. This obviated dead space correction, Tissot rinsing, and errors from changing dead space due to water evaporation and changing spirometer position.

Ambient Air Bronchospirometry.—Preoperative bronchospirometry was carried out in thirty-one of the forty patients studied. Four patients were not seen until shortly after operation; routine preoperative bronchoscopy revealed an entirely obliterated main stem bronchus in two patients, and three patients had ulcerative endobronchial disease in the left main stem bronchus. Nine patients were therefore excluded.

*This instrument can be obtained from Warren E. Collins, Inc., 555 Huntington Ave., Boston, Mass.

Recording bronchospirometry with patients breathing room air was made possible by use of a twin spirometer fitted with two balloon-box attachments described above. The connections between boxes and spirometers were made in such a way that either room air or oxygen could be supplied to either lung by the turn of a single valve.* During the course of this and other studies, good evidence was obtained that oxygen spirometry places a greatly damaged lung at a relative advantage. The percentage of the total oxygen uptake of the diseased lung can sometimes be overestimated during oxygen bronchospirometry, and we have therefore preferred ambient air bronchospirometry.[11]

Differential Total Lung Capacity.—Ambient air spirometry made it possible to determine the correct spirometer tube position, oxygen uptake, ventilation, and vital capacity without contaminating the lungs with oxygen. The procedure could therefore be followed immediately by determination of functional residual volume of both lungs separately using one open circuit apparatus for each lung. The efficiency of intrapulmonary mixing could be estimated by collection of alveolar samples of each lung separately at the end of the seven-minute oxygen breathing period.[11] The entire procedure required intubation for twelve to fifteen minutes. Difficulty with this technique was encountered because of changes in the catheter's position during oxygen breathing.[15] During the past year the use of a Carlens catheter[16] with its rubber leg engaging the carina has greatly facilitated this procedure. From the differential residual volume, and the two switching error corrections, it was possible to calculate the two total lung capacities and their subdivisions.

Ventilation Studies.—The maximum breathing capacity (MBC) was obtained using a high velocity respiratory valve and a Douglas bag.[14] The best of three efforts was recorded. The gas was collected for thirty seconds, and the volume was measured in a Tissot spirometer and reported in liters per minute at 37° C.

The exercise test consisted of a level walk at the rate of 180 feet per minute.[17] The expired air was collected during the second to fourth minutes of this exercise. The volume was measured like that of the MBC, and was also reported in liters per minute at 37° C. The walking index was calculated from the equation $\frac{\text{Walking ventilation}}{\text{MBC}} \times 100$.[17]

The best of three upright vital capacity (VC) determinations was recorded. During the past year an attachment for the vital capacity spirometer was used which records not only the total vital capacity but also, and simultaneously, the volume of air expired during the first, the first two, and the first three seconds of the effort.[18]* These timed volumes were reported as per cent of the total vital capacity. Normal volunteers and patients without obstructive ventilatory defect were able to expire on the average 83 per cent of the total vital capacity in the first second, 94 per cent in the first two seconds, and 97 per cent in the first three seconds.[18] The predicted MBC and VC were calculated from Cour-

*This instrument can be obtained from Warren E. Collins, Inc., 555 Huntington Ave., Boston, Mass.

nand's regression formulas.[13] One-half of the predicted value was used as "normal" for patients after pneumonectomy. The air velocity index was calculated from the equation $\frac{\text{per cent of predicted MBC}}{\text{per cent of predicted VC}}$.[19] This index should be 1.0 or larger in the absence of any obstructive ventilatory defect.[19]

The supine vital capacity and its subdivisions, minute ventilation, minute oxygen uptake, and respiratory rate were obtained by closed spirometry. The ventilatory equivalent for oxygen was calculated from the equation $\frac{\text{minute ventilation in liters.}}{\text{minute oxygen uptake in c.c.}}$. It was reported as number of liters ventilated per 100 c.c. oxygen removed.

Distributional and Diffusional Factors.—A rough measure of the adequacy of intrapulmonary mixing was obtained from the nitrogen content of the alveolar sample after seven minutes' oxygen breathing.[12] In normal subjects this sample contains no more than 2.5 per cent nitrogen. Cournand and associates recently observed that this value is even lower after pneumonectomy.[4] Moderate hyperventilation during the oxygen breathing period and a greatly reduced dead space and functional residual volume probably accounts for this. From data of the present investigation it was concluded that in patients after pneumonectomy an alveolar nitrogen content of over 1.5 per cent should be considered indicative of defective intrapulmonary mixing.

Early in the study, arterial samples were obtained and analyzed for oxygen and carbon dioxide content and oxygen combining power, and the arterial oxygen saturation was calculated. These studies were abandoned after a few months, chiefly because all resting oxygen saturations were well within normal limits. A large number of patients of this group were operated upon for tuberculosis, and it was felt that exercise severe enough to demonstrate arterial unsaturation was contraindicated. Finally a number of patients who gladly volunteered for ventilation studies hesitated to return to the laboratory for weekly or monthly arterial punctures.

Nomenclature.—The new definitions recently proposed by a committee of respiratory physiologists were adopted because they are simple and self-explanatory.[20] The subdivisions of the *total lung capacity* were (1) the *tidal volume* moved during resting ventilation, (2) the *inspiratory capacity* or maximal volume of inspired air measured from the pulmonary mid position, (3) the *expiratory reserve* or maximal volume of expired air measured from the pulmonary midposition, (4) the *residual volume* remaining in the lungs after maximal expiration, and (5) the *functional residual capacity* obtained by addition of the expiratory reserve and residual volume.

CLINICAL MATERIAL AND STUDY PROGRAM

Patients were selected in whom pneumonectomy was planned for disease other than primary or metastatic malignant tumor. Operation was performed for tuberculosis in thirty-five patients, for multiple lung abscesses in two, for total bronchiectasis in one, and for myoblastoma in one. Pneumonectomy and

pleurectomy were performed in one patient for total mixed empyema with multiple bronchopleural fistulas.

Nine patients had additional collapse of the remaining lung. Pneumoperitoneum was induced prior to operation and maintained throughout the period of study in eight patients. One patient had a five-rib thoracoplasty over the remaining lung prior to pneumonectomy. The functional effects of the pneumoperitoneum were ignored in the present statistical analyses because we were chiefly concerned with changes in function and the pneumoperitoneum remained unchanged both before and after operation. Furthermore, the changes due to pneumoperitoneum in patients with pneumonectomy are extremely small.[5]

No patient had significant disease from a functional standpoint of the remaining lung either before or after operation. Spreads in this series, when they occurred immediately after surgery, invariably disappeared within two to four months and were thought to have no measurable effect on pulmonary ventilation.

All but four patients were studied immediately prior to operation and all patients were studied one and two weeks, and two, three, four, and six months after operation, and every six months thereafter. Only patients studied at least six months after operation were included in the study. The walking test was omitted for the first four months after operation in all patients with tuberculosis. The MBC and upright VC tests were omitted at the one week postoperative study. One patient, after having been well for two years, suddenly developed a tuberculous abscess of the chest wall and died, presumably of miliary tuberculosis, shortly thereafter. All of the remaining thirty-nine patients are essentially well six months to two and one-half years after operation.

TREATMENT OF DATA

Each time a patient was studied, a total of twenty-two determined and derived values were obtained, excluding the preoperative bronchospirometry and differential residual volume determination. The forty patients were studied on 343 occasions, and 8,918 data were obtained. It was not possible to show these either in tabular form or in illustrations. The data were therefore presented in two ways. Typical patients' data are shown for every one of the various methods of treatment of the pneumonectomy side. In addition, statistical data are presented in summary form for each method of treatment. The number of patients in some groups was small, and still fewer patients were studied at the longer time intervals. The summary illustrations were thereby limited to one and one-half years after operation.

1. *Pneumonectomy Without Aftertreatment.*—Twelve patients received no further treatment of the empty hemithorax after resection except for two or three thoracenteses during the first postoperative week for pressure adjustment and removal of excess fluid. Penicillin and streptomycin were injected daily for two weeks.

CASE 1.—*Little Postoperative Overdistention.*—M. B., a 27-year-old woman, was operated on for tuberculosis with a completely destroyed lung (Fig. 3, Table I).

TABLE I. PNEUMONECTOMY WITHOUT AFTERTREATMENT, LITTLE OVERDISTENTION (PATIENT M. B.)

	PREOPERATIVE					POSTOPERATIVE							
FUNCTION TEST	BRON. SPIR. RIGHT	TOTAL	ONE LUNG PRED.	LEFT	RIGHT	1 WK. RIGHT	2 WK. RIGHT	2 MO. RIGHT	3 MO. RIGHT	4 MO. RIGHT	6 MO. RIGHT	1 YR. RIGHT	1½ YR. RIGHT
MBC, L./min.	--	66	43	0	66	--	53	63	64	61	60	57	59
Upright VC., c.c.	--	1,720	1,525	0	1,720	--	1,330	1,700	1,730	1,700	1,760	1,690	1,680
Air velocity index	--	1.37	1.0	-	1.37	--	1.41	1.30	1.30	1.27	1.21	1.20	1.34
Walking ventil., L./min.	--	20	15.2	0	20	--	--	--	--	--	20	20	20
Walking index, %	--	30	36	-	30	--	38	32	31	33	33	35	40
Basal resp. rate	19	19	--	-	19	24	21	20	20	20	20	18	19
Tidal volume, c.c.	100%	380	--	0	380	380	420	380	365	370	375	400	405
Inspir. capacity, c.c.	100%	1,350	--	0	1,350	1,190	1,190	1,280	1,280	1,300	1,180	1,250	1,350
Expiratory reserve, c.c.	100%	240	--	0	240	90	110	200	180	200	230	220	240
Vital capacity, c.c.	100%	1,590	1,525	0	1,590	1,280	1,300	1,480	1,460	1,500	1,410	1,470	1,590
Residual volume, c.c.	100%	560	380	0	560	300	410	630	600	670	660	720	740
Total lung capacity, c.c.	100%	2,150	1,905	0	2,150	1,580	1,710	2,110	2,060	2,170	2,070	2,190	2,330
RV/TC × 100, %	26	26	20	-	26	19	24	30	29	31	32	33	32
Ventilation, L/min.	100%	7,180	--	0	7,180	9,160	8,880	7,620	7,300	7,460	7,520	7,210	7,620
Oxygen uptake, c.c./min.	100%	240	--	0	242	251	232	219	226	230	243	236	277
Ventil. equiv. L./100 c.c.	3.0	3.0	2.2	0	3.0	3.7	3.8	3.5	3.2	3.2	3.1	3.1	2.8
Mixing index, $\%N_2$	4.67	4.67	--	-	4.67	0.63	0.88	0.62	0.81	1.76	1.11	0.92	0.65

Bronchospirometry showed no ventilation or gas exchange by the left lung. Both the VC and the MBC were larger than 50 per cent of predicted, and the air velocity index was 1.37. The residual volume and total capacity were also larger than the predicted normal for one lung. The lung was therefore somewhat hyperinflated during all phases of respiration. Residual volume expressed as per cent of total capacity (RV/TC × 100) was 26 per cent or essentially within normal limits. The pulmonary mixing index of 4.67 was greatly elevated, probably because the atelectatic and excavated left lung was not ventilated but did have nitrogen containing dead space.

Immediately after operation all components of the total capacity were decreased. The expiratory reserve suffered most, due to hesitation by the patient to make a painful forced expiration. The residual volume was reduced more than the total capacity and the RV/TC ratio was decreased to slightly below the predicted figure. These immediate postoperative findings were characteristic for all patients after primary pneumonectomy. The total capacity was reduced both because pain inhibited maximal inspiration and because the lung was somewhat compressed by large quantities of fluid and air under neutral pressure in the empty hemithorax. The respiratory rate, the minute ventilation, the ventilatory equivalent for oxygen, and the minute oxygen uptake were all increased. As the tidal volume decreased, respiration became less efficient because the dead space occupied a relatively larger portion of each breath. This patient breathed 3.7 liters for every 100 c.c. of oxygen removed, whereas only 3.0 liters of air were required before operation.

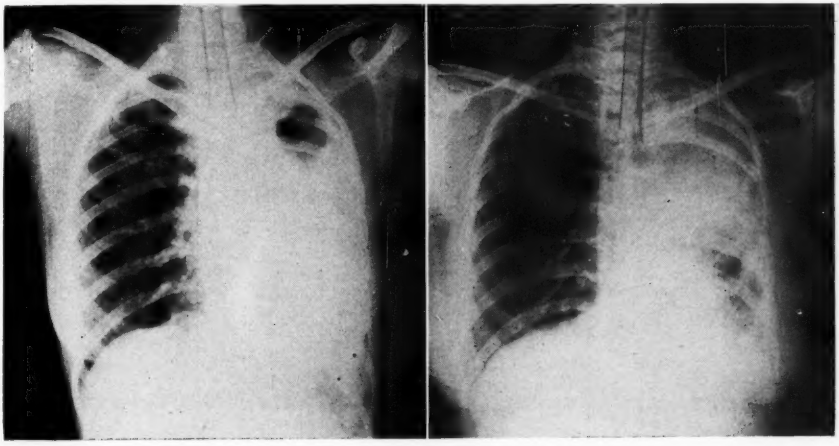

Fig. 3.—Roentgenograms of the chest of patient M. B. before operation and two years after pneumonectomy. Little overdistention was noted without further treatment.

During the following two months the total capacity returned to its preoperative level, and the vital capacity remained reduced by about 100 c.c. at the expense of the residual volume which increased about 100 c.c. The lung at full inspiration was no more overdistended than before operation (Fig. 3), but the resting or midposition at the end of a quiet expiration was somewhat higher. This increase of the RV/TC ratio to 30 per cent is sometimes considered to represent slight emphysema.[21, 22]

During the next one and one-half years no further striking changes occurred. The oxygen uptake increased as the patient gained 45 pounds, and minute ventilation and the ventilatory equivalent returned to the preoperative values. The pulmonary mixing index was sharply reduced immediately after operation, and never increased above 1.76 per cent nitrogen after that.

TABLE II. PNEUMONECTOMY FOLLOWED BY MARKED OVERDISTENTION AND EARLY THORACOPLASTY (PATIENT R. M.)

	PREOPERATIVE					AFTER PNEUMONECTOMY				AFTER THORACOPLASTY			
FUNCTION TEST	BRON. SPIR. LEFT	TOTAL	ONE LUNG PRED.	RIGHT	LEFT	1 WK. LEFT	2 WK. LEFT	2 MO. LEFT	3 MO. LEFT	2 WK. LEFT	2 MO. LEFT	4 MO. LEFT	1 YR. LEFT
MBC, L./min.	--	52	48	--	--	--	41	43	43	38	39	31	36
Upright VC, c.c.	--	1,900	1,540	--	--	--	1,560	1,560	1,550	1,250	1,350	1,300	1,590
Air velocity index	--	0.87	1.0	--	--	--	0.84	0.90	0.90	0.98	0.93	0.76	0.73
Walking ventil., L./min.	--	12	16	--	--	--	--	--	--	--	--	.15	.14
Walking index %	--	23	34	--	--	--	29	28	28	31	32	49	38
Basal resp. rate	15	15	--	15	15	22	18	14	14	18	14	15	15
Tidal volume, c.c.	78%	360	--	80	280	330	365	420	400	340	380	340	370
Inspir. capacity, c.c.	86%	1,600	--	220	1,380	1,210	1,400	1,370	1,350	1,160	1,160	1,155	1,250
Expiratory reserve, c.c.	100%	100	--	0	100	0	90	105	100	100	120	125	105
Vital capacity, c.c.	87%	1,700	1,540	220	1,480	1,210	1,490	1,475	1,450	1,260	1,280	1,280	1,355
Residual volume, c.c.	66%	595	385	200	395	270	370	725	760	390	400	380	435
Total lung capacity, c.c.	82%	2,295	1,925	420	1,875	1,480	1,860	2,200	2,210	1,650	1,680	1,660	1,790
RA/TC × 100, %	21	26	20	48	21	18	20	33	34	24	24	23	24
Ventilation, L./min.	78%	5,420	--	1,210	4,210	7,300	6,550	5,880	5,600	6,080	5,320	5,090	5,530
Oxygen uptake, c.c./min.	89%	226	--	25	201	261	234	228	208	230	205	215	254
Ventil. equiv. L./100 c.c.	2.1	2.4	2.2	4.8	2.1	2.8	2.8	2.6	2.7	2.6	2.6	2.4	2.2
Mixing index, % N_2	1.06	2.12	--	5.71	1.06	0.52	0.34	1.06	1.26	0.68	0.38	0.92	0.67

Studies of this patient illustrate that (1) overdistention occurs chiefly during the first two months after operation (2) overdistention postoperatively remains minimal in certain patients, and (3) pneumonectomy for a functionless lung causes no further loss of maximal function as expressed by MBC and VC.

CASE 2.—*Early Severe Postoperative Overdistention:* R. M., a 24-year-old woman, had a pneumonectomy for giant tension cavity which developed during induction of an unsuccessful pneumothorax for far advanced cavernous pulmonary tuberculosis (Fig. 4, Table II).

Preoperative bronchospirometry and differential lung volume determination showed that oxygen uptake of the right lung was reduced to 11 per cent of the total. Ventilation and vital capacity were almost equally reduced. The residual volume on the right was only slightly reduced and the RV/TC ratio was 48 per cent. This does not indicate emphysema, but merely shows that little of the air within the lung could be expired on maximal effort. The mixing index of 5.71 per cent on that side was greatly elevated. The "good" lung showed a normal relationship of the various components of the total capacity, although all components were somewhat less than 50 per cent of predicted. This patient, unlike the last one, had a slightly smaller than normal lung, perhaps because of the pneumoperitoneum and previous cavernous disease on that side.

Fig. 4.—Roentgenograms of the chest of patient R. M. before and three months after pneumonectomy. Severe overdistention occurred soon after operation.

Immediately after operation this patient's studies duplicated those of the last patient (M.B.). All components of the total capacity were reduced. As in the last case, ventilation became more inefficient due to increased respiratory rate and decreased tidal volume.

Beginning the second week after operation, the studies of this patient began to show great differences from the previous case. The vital capacity showed no further improvement, but the total capacity increased steadily due to a rising residual volume. At the end of two months, the residual volume was 130 c.c. larger than the combined residual volume before operation and 330 c.c. larger than the residual volume of the "good" lung alone. The RV/TC ratio had nearly doubled (Table II, Fig. 4). Since the right lung participated to some extent in ventilation, its removal, unlike in the last patient, caused a permanent reduction of VC and MBC. Because of these findings, an early thoracoplasty was performed. Changes following this procedure will be discussed later.

TABLE III. PNEUMONECTOMY WITHOUT AFTERTREATMENT, PREOPERATIVE OVERDISTENTION (PATIENT W. H.)

	PREOPERATIVE					POSTOPERATIVE							
FUNCTION TEST	BRON. SPIR. LEFT	TOTAL	ONE LUNG PRED.	RIGHT	LEFT	2 WK. LEFT	2 MO. LEFT	3 MO. LEFT	4 MO. LEFT	6 MO. LEFT	1 YR. LEFT	1½ YR. LEFT	2 YR. LEFT
MBC, L./min.	--	56	47	--	--	40	42	49	49	50	49	45	44
Upright VC, c.c.	--	2,410	1,840	--	--	1,720	1,900	2,020	2,030	2,060	2,030	2,030	2,030
Air velocity index	--	0.92	1.0	--	--	0.92	0.81	0.95	0.95	0.95	0.95	0.87	0.84
Walking ventil., L./min.	--	25	15	--	--	--	--	--	--	--	13	18	--
Walking index %	--	45	32	--	--	62	60	57	57	50	27	39	40
Basal resp. rate	17	17	--	17	17	--	23	19	18	18	17	21	20
Tidal volume, c.c.	77%	375	--	85	290	--	370	390	350	340	365	460	340
Inspir. capacity, c.c.	93%	1,070	--	75	995	--	790	840	900	860	840	830	975
Expiratory reserve, c.c.	87%	1,130	--	145	985	--	930	960	920	860	1,020	1,020	905
Vital capacity, c.c.	90%	2,200	1,840	220	1,980	--	1,720	1,800	1,820	1,720	1,860	1,850	1,880
Residual volume, c.c.	87%	1,570	565	205	1,365	--	1,140	1,150	1,320	1,190	1,400	1,420	1,085
Total lung capacity, c.c.	89%	3,770	2,405	425	3,345	--	2,860	2,950	3,140	2,910	3,260	3,270	2,965
RV/TC × 100, %	41	42	23.4	48	41	--	40	39	42	41	43	43	37
Ventilation, L./min.	77%	6,360	--	1,460	4,900	--	8,675	7,400	6,350	6,100	6,180	9,640	6,830
Oxygen uptake, c.c./min.	96%	201	--	7	194	--	228	231	205	218	216	290	222
Ventil. equiv. L./100 c.c.	2.5	3.2	2.2	20.8	2.5	--	3.8	3.2	3.1	2.8	2.9	3.3	3.1
Mixing index, % N_2	--	--	--	--	--	--	3.10	2.56	1.98	3.46	3.64	3.73	4.32

This study illustrates that (1) overdistention occurs early after operation, (2) overdistention can be rapid and severe in certain patients, and (3) removal of a lung participating in ventilation to any extent causes a permanent loss of maximal ventilatory function.

CASE 3.—*Overdistention and Emphysema Before Operation:* W. H., a 42-year-old Negro man, had been treated for pulmonary tuberculosis for four years prior to operation. He had a manic-depressive episode immediately after operation, and the one- and two-week studies could not be performed.

Prior to operation, bronchospirometry revealed an almost entirely destroyed lung on the right (Fig. 5, Table III). Differential residual volume determination showed only 11 per cent of the total capacity on the right, and almost one-half of this was residual volume. The "good" lung before operation was greatly overdistended. It alone occupied a space (3,345 c.c.) which was over two-thirds of the total predicted volume (4,810

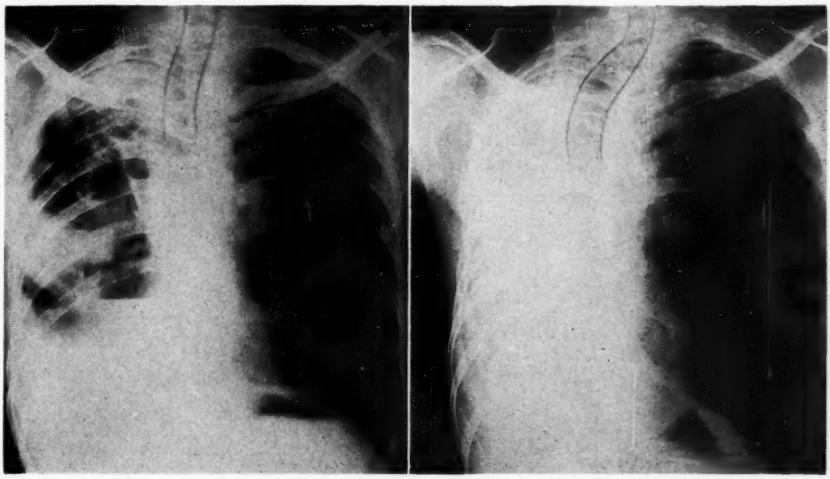

Fig. 5.—Roentgenograms of the chest of patient W. H. before and three years after pneumonectomy. The overdistention prior to resection was marked.

c.c.). The single vital capacity was just 50 per cent of the total predicted, but the residual volume was nearly twice normal. The RV/TC ratio of the "good" lung alone was increased to 41 per cent. In this patient, this represented true emphysema in part. The timed capacities during the first, the first two, and the first three seconds obtained from the spirogram were only 58, 68, and 77 per cent of the total vital capacity, respectively, showing a definite slowing of the air stream. Further evidence of an obstructive ventilatory defect was given by the air velocity index of less than 1.0. This index is usually higher than 1.0 in patients with chronic loss of ventilating lung tissue without obstructive elements.[19]

Comparison of the total capacity of the single "good" lung before operation with that during the two years after operation shows essentially no change. No further overdistention occurred. This patient's studies are unusual in three respects. Unlike all other patients, this subject's inspiratory capacity was smaller than his expiratory reserve which was relatively huge. The functional residual volume was therefore greatly elevated. The patient breathed with a greatly overdistended lung which is only partly expressed by the RV/TC ratios of 37 to 43 per cent. The mixing index was much larger than the

normal 1.5 per cent nitrogen after pneumonectomy. This patient was also unusual in that he showed evidence of true emphysema which increased during the second year of study. The MBC showed a progressive decline, the air velocity index and breathing reserve during exercise decreased also, and the timed capacities declined while the total vital capacity remained unchanged.

In summary, this patient showed that (1) postoperative overdistention need not necessarily be the result of the removal of the lung, but may have been present to an equal extent prior to operation and (2) that simple overdistention may, at an early date, develop into true obstructive emphysema.

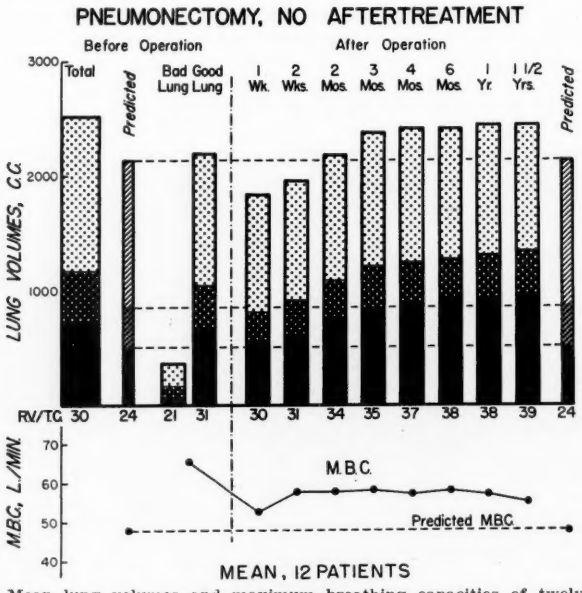

Fig. 6.—Mean lung volumes and maximum breathing capacities of twelve patients not further treated after pneumonectomy. The total lung capacities and subdivisions of both lungs together and each lung separately are shown before operation and at intervals thereafter. The predicted lung volume and maximum breathing capacity for a single lung are indicated. The subdivisions of the total lung capacity in this and subsequent drawings are identified as follows: black: residual volume, stippled black: expiratory reserve, stippled white: inspiratory capacity. The two dark areas together represent the functional residual capacity and the two stippled areas together represent the vital capacity.

Fig. 6 shows a summary of studies of twelve patients who had no further treatment after pneumonectomy. Before operation the average "good" lung showed a normal total capacity, a somewhat reduced vital capacity, and a slightly increased residual volume. Therefore, slight overdistention was present during quiet respiration, but not at fullest inspiration. When compared to the single "good" lung before operation, the inspiratory capacity and expiratory reserve, together the vital capacity, showed a sharp decrease shortly after operation and returned to their preoperative values within two months. The total capacity showed a slight decrease immediately after operation but then increased during the first few months. This increase was entirely due to a sharp increase of the residual volume from 681 c.c. before operation to 903 c.c. four months after pneumonectomy. The RV/TC ratio increased from 31 to 37 per cent. Thus, after operation the average lung was somewhat overdistended both in maximal inspiration and in the pulmonary midposition, more so in the latter.

2. *Pneumothorax.*—In six patients, the fluid was removed from the space formerly occupied by the lung and replaced with air. These patients were selected because their condition was so poor prior to pneumonectomy that it was thought unlikely that they would soon thereafter be able to tolerate further surgery. The space was dried by thoracentesis immediately after operation and every day thereafter for fourteen days. Thoracenteses were followed by streptomycin and penicillin injections. Usually no further punctures were necessary after this time. Pressures were maintained slightly on the negative side for two weeks. The amount of weekly refills was then governed by the position of the mediastinum seen by fluoroscopy and by reports of lung volumes from the laboratory. Neutral mean pressures usually sufficed for the first month, and

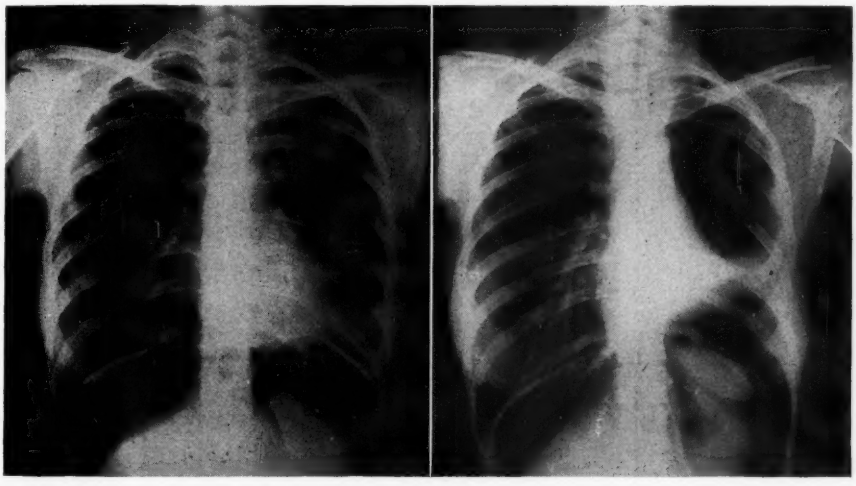

Fig. 7.—Roentgenograms of the chest of patient A. L. before pneumonectomy and six months after pneumothorax treatment of the space. No overdistention was observed.

mean pressures of plus 3 and plus 5 cm. of water were needed thereafter. In one patient, reappearance of clear yellow fluid four months after operation was indicative of tuberculous empyema. This was first treated by lavage and later by oleothorax.

Case 4.—A. L., a 23-year-old woman, had a pneumonectomy for multiple tuberculous excavations in both lobes of the left lung (Fig. 7). The patient was very ill and toxic, and weighed only eighty-six pounds.

Bronchospirometry prior to operation showed that the left lung contributed about one-fourth of the total ventilation, oxygen uptake and vital capacity; differential residual volume determination showed 35 per cent of the total residual volume on the left (Table IV). In spite of the advanced disease, the MBC was 108 per cent of predicted for two lungs, and the upright VC was 100 per cent of predicted. The "good" right lung was much larger than expected. Its total capacity was 136 per cent of the calculated normal volume. However, the components of this total capacity had a normal relationship, and the RV/TC ratio was 20 per cent (normal).

TABLE IV. PNEUMONECTOMY FOLLOWED BY PNEUMOTHORAX (PATIENT A. L.)

	PREOPERATIVE					POSTOPERATIVE					
FUNCTION TEST	BRON. SPIR. RIGHT	TOTAL	ONE LUNG PRED.	LEFT	RIGHT	1 WK. RIGHT	2 WK. RIGHT	2 MO. RIGHT	3 MO. RIGHT	4 MO. RIGHT	6 MO. RIGHT	1 YR. RIGHT
MBC, L./min.	--	98	46	--	--	--	70	79	81	83	82	83
Upright VC, c.c.	--	2,910	1,465	--	--	--	2,260	2,240	2,240	2,260	2,270	2,230
Air velocity index	--	1.09	1.00	--	--	--	1.00	1.16	1.19	1.20	1.18	1.20
Walking ventil., L./min.	--	17	15.2	--	--	--	--	--	--	--	17	17
Walking index, %	--	17	34	--	--	--	24	22	22	20	21	21
Basal resp. rate	19	19	--	19	19	23	19	17	17	17	16	16
Tidal volume, c.c.	--	340	--	80	260	365	405	345	335	355	325	375
Inspir. capacity, c.c.	67%	1,950	--	635	1,315	1,270	1,410	1,400	1,450	1,440	1,410	1,475
Expiratory reserve, c.c.	100%	690	--	0	690	260	300	420	460	450	440	525
Vital capacity, c.c.	76%	2,640	1,465	635	2,005	1,530	1,710	1,820	1,910	1,890	1,850	2,000
Residual volume, c.c.	65%	750	365	260	730	310	370	450	450	470	490	510
Total lung capacity, c.c.	74%	3,390	1,830	895	2,495	1,840	2,080	2,270	2,360	2,360	2,340	2,510
RV/TC × 100, %	20	22	20	29	20	17	18	20	19	20	21	20
Ventilation, L./min.	76%	6,500	--	1,700	4,800	8,440	7,570	5,880	5,700	6,030	5,240	6,020
Oxygen uptake, c.c./min.	80%	224	--	45	179	248	244	226	228	232	218	242
Ventil. equiv. L./100 c.c.	2.7	2.9	2.2	3.8	2.7	3.4	3.1	2.6	2.5	2.6	2.4	2.5
Mixing index, % N_2	--	1.84	--	1.06	2.27	0.62	0.81	0.76	0.94	0.47	0.92	0.71

Immediately after operation, the changes were the same as in the previous cases. All components of the total capacity were reduced, the residual volume more so than the others, probably due to high pneumothorax pressures.

During the first postoperative year, an entirely different picture developed than in the patients without treatment. At the end of three months, all components of the total capacity had regained the values of the single "good" lung before operation, and the normal relationship between vital capacity and residual volume persisted. This RV/TC ratio remained normal throughout the period of study. The preoperative residual volume

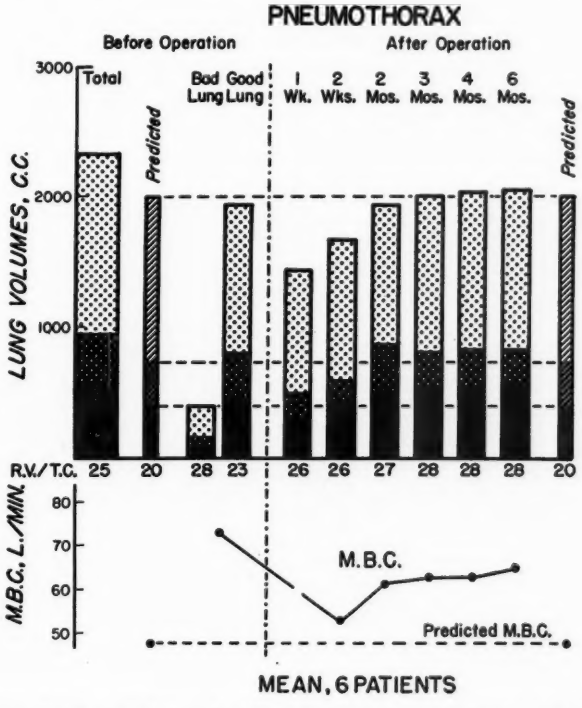

Fig. 8.—Mean function studies of 6 patients in whom pneumonectomy was followed by pneumothorax.

of the single lung was 490 c.c., and this same volume was 510 c.c. one year later. Maximal preservation of function of the remaining lung was further shown by a maximum breathing capacity, which was 182 per cent of the normal predicted for one lung and by a vital capacity of 152 per cent of predicted. Although this patient's lung was much larger than predicted, it also functioned much better in every respect. Since the RV/TC ratio remained normal, this large size could not be regarded as evidence of overdistention, but rather as the remaining lung of a patient with unusually good pulmonary function prior

Fig. 8 shows a summary of the postoperative studies of six patients maintained on pneumothorax. The immediate postoperative changes were the same as in the previous chart. At the end of three months there was no evidence of overdistention and, although the residual volume slowly increased, at the end of one year it was only 80 c.c. larger than the calculated single residual volume before operation. The RV/TC ratio increased only 4 per cent. The MBC was

TABLE V. PNEUMONECTOMY FOLLOWED BY OLEOTHORAX (PATIENT D. D.)

	PREOPERATIVE					POSTOPERATIVE, PNEUMOTHORAX					OLEOTHORAX		
FUNCTION TEST	BRON. SPIR. RIGHT	TOTAL	ONE LUNG PRED.	LEFT	RIGHT	1 WK.* RIGHT	2 WK. RIGHT	2 MO. RIGHT	3 MO. RIGHT	4 MO. RIGHT	6 MO. RIGHT	1 YR. RIGHT	1½ YR. RIGHT
MBC, L./min.	--	58	40	--	--	--	42	46	45	46	45	45	39
Upright VC, c.c.	--	1,980	1,570	--	--	--	1,250	1,510	1,490	1,500	1,500	1,500	1,450
Air velocity index	--	1.16	1.00	--	--	--	1.33	1.19	1.18	1.21	1.19	1.19	0.94
Walking ventil., L./min.	--	16	14	--	--	--	--	--	--	--	16	--	16
Walking index, %	--	27	34	--	--	--	38	35	36	35	36	37	36
Basal resp. rate	15	15	--	15	15	32	16	14	14	13	13	15	14
Tidal volume, c.c.	72%	430	--	110	320	210	410	370	330	370	330	415	320
Inspir. capacity, c.c.	77%	1,360	--	310	1,050	590	870	1,015	1,000	980	1,110	1,015	965
Expiratory reserve, c.c.	76%	340	--	80	260	0	140	210	210	200	225	230	225
Vital capacity, c.c.	77%	1,700	1,570	390	1,310	590	1,010	1,225	1,210	1,180	1,335	1,245	1,190
Residual volume, c.c.	69%	540	390	170	370	210	430	585	570	580	625	615	560
Total lung capacity, c.c.	75%	2,240	1,960	560	1,680	800	1,440	1,810	1,780	1,760	1,960	1,860	1,750
RV/TC × 100, %	22	24	20	30	22	26	30	32	32	33	32	33	32
Ventilation, L./min.	72%	6,440	--	1,800	4,640	6,510	6,570	5,170	4,580	4,780	4,310	6,220	4,490
Oxygen uptake, c.c./min.	78%	201	--	42	159	217	212	196	203	201	192	200	192
Ventil. equiv., L./100 c.c.	2.9	3.3	2.2	4.3	2.9	3.0	3.1	2.6	2.2	2.4	2.2	3.1	2.3
Mixing index, % N_2	2.90	2.68	--	2.90	1.70	--	1.20	--	1.10	1.42	1.67	1.95	1.30

*Spontaneous pneumothorax of remaining lung.

138 per cent of the "one lung" predicted, and the VC was 94 per cent of this same value.

Pneumothorax completely confined the remaining lung within its normal position and volume, and it did so without causing any further reduction of maximal ventilation.

3. *Oleothorax.*—Two patients were maintained on pneumothorax for four and nine months, respectively, and the space was then filled with oil. This was done in one patient because of the appearance of clear yellow fluid containing *M. tuberculosis,* and in the other, because of appearance of sterile cloudy fluid. A third patient, not included in this series, has been followed for three years with oleothorax on one side and an extrapleural pneumothorax of the remaining lung.[5] The oil in the first two cases was mineral oil, and in the last case, olive oil. Formation of fluid subsided in the first two patients shortly after introduction of the oil, and all three patients are well at present.

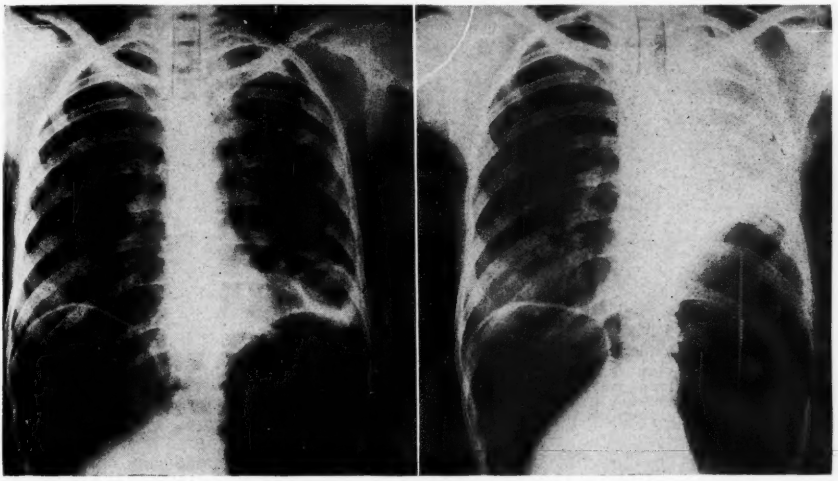

Fig. 9.—Roentgenograms of the chest of patient D. D. before pneumonectomy and one year after induction of oleothorax. No overdistention was observed.

CASE 5.—D. D., a 26-year-old woman, had a pneumonectomy for multiple excavation of the upper lobe of the left lung and a single large cavity just above the left diaphragm (Fig. 9). The patient did well on pneumothorax treatment of the space formerly occupied by the left lung. After four months a tuberculous empyema developed and the space was filled with mineral oil.

Unlike the previously discussed cases, this patient's single "good" lung before operation was smaller than predicted (Table V). The VC was 1,310 c.c. (predicted 1,570) and the residual volume was 370 c.c. (predicted 390 c.c.). The RV/TC × 100 ratio was normal, that is, the lung was not overdistended in the pulmonary midposition. The lung to be resected showed remarkably good function in spite of extensive cavitation. It was responsible for about one-fourth of the total ventilation and oxygen uptake at rest.

One week after operation the patient developed a spontaneous pneumothorax of the one remaining lung. At that time, the VC was only 590 c.c., and the total lung volume was only 800 cubic centimeters. Complete re-expansion was accomplished at the end of

two weeks. At that time, the usual immediate postoperative changes were observed. After two months, the VC had regained its preoperative value but the residual volume had increased to 585 c.c., and the RV/TC ratio was elevated to 30 per cent. Thus, at deepest inspiration, the lung was still smaller than the single predicted lung volume, but during quiet breathing the lung was slightly overdistended. No further change occurred during the next two months. At the end of four months, the space was filled with oil (Table V). This caused no further change of maximal ventilation as expressed by the MBC. The total lung capacity also remained entirely unchanged and there was no alteration in the relationship of the subdivisions of the total capacity. No further change occurred during the course of the next one and one-half years.

Oleothorax replacing pneumothorax as lung prosthesis caused no further change of maximal ventilation and no alteration of the total capacity and its subdivisions.

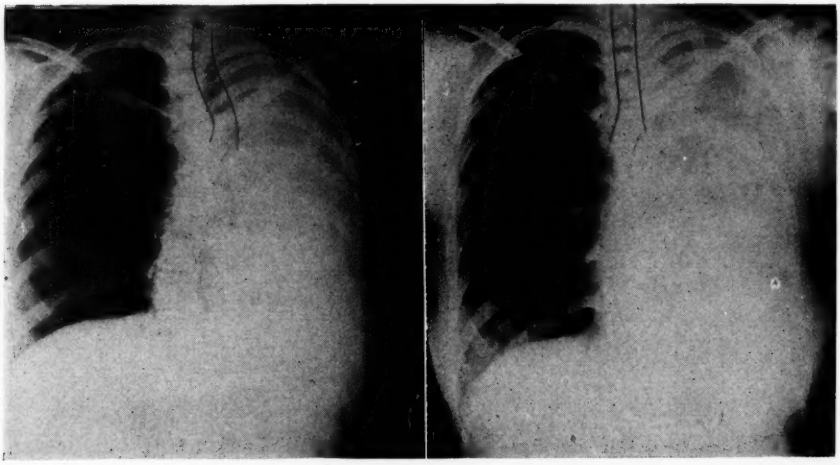

Fig. 10.—Roentgenograms of the chest of patient F. Z. before pneumonectomy and four months after introduction of a plastic sponge into the space. The overdistention existing before operation has been corrected.

4. *Plastic Sponge Plombage.*—In three patients, the space was maintained as a pneumothorax for three to nine months, and a plastic sponge prosthesis was then introduced. The sponge (Ivalon) was used by Grindley and Clagett in experimental animals and was found to be relatively inert.[23] Its use in man has not been recorded previously. From one to three sponges were shaped roughly to fit the space, soaked in a penicillin-streptomycin solution and introduced through the fourth intercostal space. A small amount of fluid was removed on a few occasions during the first two weeks after operation. The spaces then remained dry, and the structural detail of the sponges was visible on the roentgenogram.

CASE 6.—F. Z., a 24-year-old woman, was admitted with a completely atelectatic left lung (Fig. 10). Severe ulcerative endobronchial disease was noted on bronchoscopy of the left mainstem bronchus, and the bronchus was completely occluded by scarring, stricture, and edema proximal to the take-off of the left upper lobe. The left lung was removed, and the space was maintained as a pneumothorax for two months. At that time the major portion of three sponges, measuring 3 by 4 by 7 inches, was introduced into the space. The postoperative course was uneventful.

Both the preoperative roentgenogram (Fig. 10) and the preoperative lung volume studies (Table VI), showed marked overdistention of the functioning lung. This overdistention, however, had not taken place in the residual volume fraction of the total capacity. All components of the total capacity were proportionately enlarged, and the RV/TC ratio was therefore normal. This patient, like A. L. (Table IV), had a large well-functioning lung.

The changes observed immediately after operation and during the two months of pneumothorax treatment did not differ from those of patient A. L. Just prior to plombage the total capacity and the MBC were slightly smaller than before operation, and the residual volume was slightly larger than before.

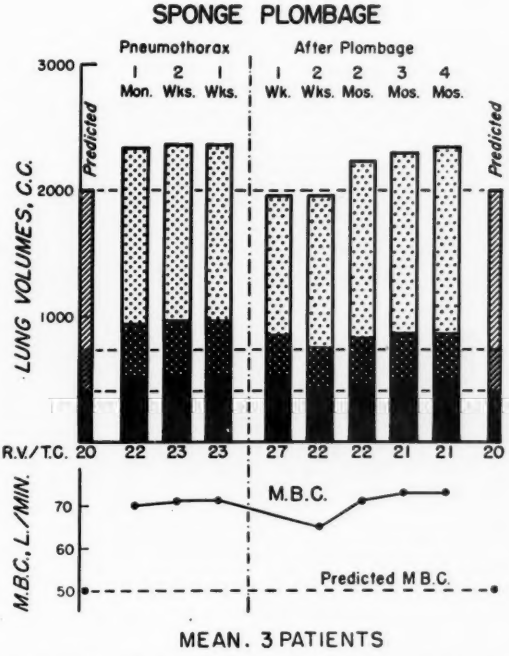

Fig. 11.—Mean function studies of three patients in whom pneumonectomy was followed by pneumothorax treatment of the space and later plastic sponge plombage.

Introduction of the sponges caused a decrease of MBC and all the components of the total capacity for only two weeks. Two months after secondary operation, the MBC, VC, and total capacity had regained the values for the single lung found before pneumonectomy. Only the residual volume remained decreased and the RV/TC × 100 percentage of 14 was the lowest recorded in this series. This was found to be due to compression of the lung by accumulation of fluid around the sponge. This fluid had never been removed after operation, and its removal now brought a return of the residual volume to its normal value seen at the end of three months.

The results of studies of three patients with sponge prostheses are summarized in Fig. 11. The changes caused by plombage are what the physiologist might consider as "ideal." The stroke volume as expressed by the vital capacity and the maximal ventilation as expressed by the MBC remained unchanged, and

TABLE VI. PNEUMONECTOMY FOLLOWED BY PNEUMOTHORAX AND LATER PLASTIC SPONGE PLOMBAGE (PATIENT F. Z.)

FUNCTION TEST	BEFORE OP.		PNEUMONECTOMY & PNEUMOTHORAX					SPONGE PLOMBAGE			
	ONE LUNG PRED.	RIGHT*	1 WK. RIGHT	1½ WK. RIGHT	2 WK. RIGHT	1 MO. RIGHT	2 MO. RIGHT	1 WK. RIGHT	2 WK. RIGHT	2 MO. RIGHT	3 MO. RIGHT
MBC, L./min.	58	60	48	50	58	59	55	--	52	58	60
Upright VC, c.c.	1,705	2,350	2,010	2,030	2,380	2,320	2,290	--	1,920	2,110	2,300
Air velocity index	1.00	0.67	0.70	0.72	0.71	0.73	0.70	--	0.81	0.80	0.84
Walking ventil. L./min.	20	28	--	--	--	--	--	--	--	--	--
Walking index, %	34	47	58	56	48	48	51	--	54	48	47
Basal resp. rate	--	14	17	18	14	13	18	26	22	21	21
Tidal volume, c.c.	--	480	440	430	445	460	355	320	290	345	350
Inspir. capacity, c.c.	--	1,710	1,450	1,450	1,640	1,830	1,600	1,330	1,390	1,820	1,920
Expiratory reserve, c.c.	--	550	405	410	420	350	350	270	225	290	350
Vital capacity, c.c.	1,705	2,260	1,855	1,860	2,060	2,180	1,950	1,600	1,615	2,110	2,270
Residual volume, c.c.	425	510	655	660	600	410	565	435	295	350	570
RV/TC × 100, %	20	18	26	26	23	15	22	21	15	14	20
Total capacity, c.c.	2,130	2,770	2,510	2,520	2,660	2,590	2,515	2,035	1,910	2,460	2,840
Ventilation, L./min.	--	6,800	7,520	7,680	6,300	6,150	6,375	8,300	6,360	7,250	7,230
Oxygen uptake, c.c./min.	--	342	238	347	236	233	255	297	230	234	232
Vent. equiv., L./100 c.c.	2.2	2.0	3.2	2.2	2.7	2.6	2.5	2.8	2.8	3.1	3.1
Mixing index, % N_2	--	1.24	2.70	1.97	1.74	1.30	1.67	0.69	0.68	0.65	0.77

*No patent left main-stem bronchus.

the residual volume was decreased sufficiently to make its ratio to the total capacity normal.

Plastic sponge plombage caused no reduction of maximal function, and confined the remaining lung within its normal space. Preoperative overdistention could be corrected by this procedure. The follow-up period was only brief.

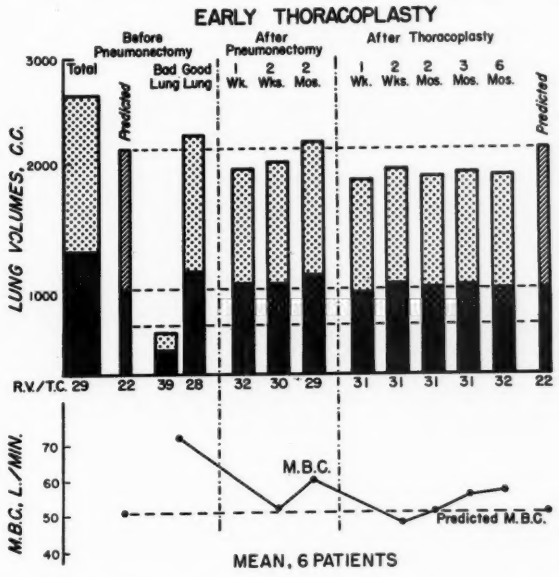

Fig. 12.—Mean function studies of six patients in whom pneumonectomy was followed by thoracoplasty six weeks to two months later.

5. *Early Thoracoplasty.*—This procedure was carried out in six patients six weeks to two months after resection. Portions of five to seven ribs were removed in one stage, not including the rib resected at the time of pneumonectomy. The first rib and the transverse processes were not disturbed to minimize deformity.

The laboratory findings in six patients before pneumonectomy, immediately after resection and after thoracoplasty are summarized in Fig. 12. The lung to be resected contributed only 20 per cent of the total lung volume before operation. The "good" lung before operation was slightly overdistended both in full inspiration and in the midposition. Changes in lung volumes and MBC during the first two months after operation differed in no way from the groups discussed previously and might be superimposed on Fig. 6, showing changes of pneumonectomy without aftertreatment. The MBC was reduced from 72 to 52 liters per minute immediately after resection, and rose to 60 liters per minute at the end of two months.

Early thoracoplasty further reduced the MBC to 48 liters per minute and six months after this operation, it had risen to 56 liters per minute, but never

TABLE VII. PNEUMONECTOMY FOLLOWED BY LATE THORACOPLASTY (PATIENT A. P.)

	PREOPERATIVE		AFTER PLEURO-PNEUMONECTOMY				AFTER THORACOPLASTY				
FUNCTION TEST	ONE LUNG PRED.	RIGHT*	1 WK. RIGHT	2 WK. RIGHT	2 MO. RIGHT	4 MO. RIGHT	1 WK. RIGHT	2 WK. RIGHT	2 MO. RIGHT	4 MO. RIGHT	1½ YR. RIGHT
MBC, L./min.	41	50	--	43	44	45	--	35	35	35	31
Upright VC, c.c.	1,430	2,030	--	1,530	1,700	1,770	--	1,530	1,540	1,540	1,210
Air velocity index	1.00	0.86	--	0.96	0.91	0.84	--	0.81	0.81	0.81	0.90
Walking ventilation, L./min.	15	17	--	--	--	--	--	--	--	--	--
Walking index, %	36	34	--	40	38	36	--	49	49	49	55
Basal resp. rate	--	21	26	22	21	24	30	28	24	23	23
Tidal volume, c.c.	--	245	260	260	240	260	190	180	210	230	220
Inspir. capacity, c.c.	--	1,520	1,050	1,250	1,330	1,290	1,175	1,150	1,165	1,180	1,130
Expiratory reserve, c.c.	--	230	160	200	220	255	200	220	210	220	195
Vital capacity, c.c.	1,430	1,750	1,210	1,450	1,550	1,545	1,375	1,370	1,375	1,400	1,325
Residual volume, c.c.	435	1,070	770	1,150	1,170	1,020	645	710	775	790	900
Total capacity, c.c.	1,865	2,820	1,980	2,600	2,720	2,555	2,020	2,080	2,150	2,190	2,225
RV/TC × 100, %	23	38	39	44	43	40	32	34	36	36	40
Ventilation, L./min.	--	5,120	6,700	5,700	5,040	6,250	5,700	5,040	5,040	5,290	5,020
Oxygen uptake, c.c./min.	--	210	249	228	242	250	275	260	235	220	230
Ventil. equiv., L./100 c.c.	2.2	2.4	2.7	2.5	2.1	2.5	2.1	1.9	2.1	2.4	2.2
Mixing index, % N_2	--	1.46	1.03	2.01	3.26	2.80	2.02	2.07	1.86	2.01	2.10

*No patent left main-stem bronchus.

regained the value found just prior to thoracoplasty. All components of the total lung capacity were permanently reduced by this secondary operation. The remaining lung six months after thoracoplasty, was smaller than the predicted. The overdistention at full inspiration was thus overcorrected. However, in the pulmonary midposition, the lung was still overdistended in spite of a reduction of the expiratory reserve. The RV/TC × 100 percentage of 32 was larger than immediately prior to thoracoplasty. Similar changes were observed in patient R. M. (Table II).

Fig. 13.—Roentgenograms of the chest of patient A. P. three months after pleuro-pneumonectomy and six months after thoracoplasty. The posterior herniation of the right lung was not corrected.

The alterations in function caused by early thoracoplasty were not entirely desirable. The maximal stroke volume as expressed by the VC was reduced, maximal ventilation tested by the MBC was permanently reduced and the residual volume still was larger than predicted. No overdistention was present on deepest inspiration, a respiratory position assumed relatively rarely. Overdistention was present in the pulmonary midposition, the size in which the lung is most frequently encountered during a sedentary life.

6. *Late Thoracoplasty.*—This operation was done in one stage five months to two years after pneumonectomy. The first rib and the transverse processes were not removed. Resection of five to nine ribs including revision of the regenerated rib removed at the time of pneumonectomy was carried out.

Case 7.—Patient A. Z., a 36-year-old woman was admitted to the Sanatorium Division with a history of tuberculous empyema following unsuccessful pneumothorax ten years ago. An acute illness characterized by expectoration of much foul sputum and high fever began one week before admission. A diagnosis of putrid empyema with bronchopleural fistula was made and the space was drained. Bronchoscopy revealed only a pin point opening of the left main-stem bronchus. Four months after admission, the entire parietal

pleura, including the lung, was removed. A posterior herniation of the contralateral lung was noted at operation. The patient made an uneventful recovery except for a permanent Horner's syndrome first noted immediately after operation.

Physiologic data are shown in Table VII. Before operation, both VC and MBC were somewhat larger than predicted. The total capacity was greatly elevated due to a residual volume of the single lung which was larger than that predicted for two normal lungs. This residual volume occupied 38 per cent of the total capacity (RV/TC × 100). The various components of the total lung capacity were reduced only at the one week interval after operation. At the end of four months, the VC was smaller than before operation but the residual volume had regained its former value and was now 44 per cent of the total capacity.

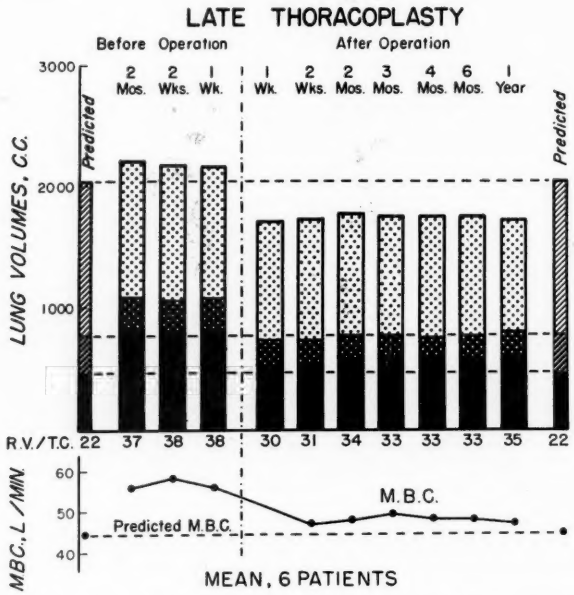

Fig. 14.—Mean function studies of six patients in whom pneumonectomy was followed by thoracoplasty six months to two years later.

Roentgenograms of the chest at this time revealed a large posterior herniation of the right lung which was also observed at the time of operation (Fig. 13). Because of the very high position of the diaphragm, a small thoracoplasty was performed. Both the physiologic data (Table VII) and the roentgenogram (Fig. 13) showed no or very slight reduction of this herniation. The lung remained overdistended both on full inspiration and in the pulmonary midposition. One and one-half years later, the residual volume still occupied 40 per cent of the total capacity.

The changes of VC and MBC after late thoracoplasty were in great contrast to those after oil and sponge plombage. There was a slight permanent reduction of stroke volume but maximal voluntary ventilatory ability, as measured by the MBC, was severely and permanently reduced from 45 to 35 liters per minute. A loss of ten liters of MBC is of no significance if the initial MBC is 100 or even 200 liters per minute. Here ten liters represented a 22 per cent decrease and the patient who had never been dyspneic before thoracoplasty, now complained of exertional dyspnea. The further reduction to 31 liters one year later may well represent the onset of true emphysema with early disruption of the pulmonary parenchymal architecture.

Fig. 14 shows the rather striking mean findings of six patients after late thoracoplasty. Two months, two weeks, and one week before thoracoplasty, the lung was moderately overdistended both on full inspiration and in the pulmonary midposition, more so in the latter. The residual volume was nearly twice normal and occupied 38 per cent of the total capacity. Thoracoplasty accomplished just the opposite of the desired result. The range of the useful respiratory movement (VC) was greatly reduced, whereas the volume which merely dilutes the inspired tidal air (residual volume) was only slightly reduced. It still occupied one-third of the total capacity. Worst of all, the initial mean MBC of 58 liters per minute was permanenty reduced to 46 liters per minute.

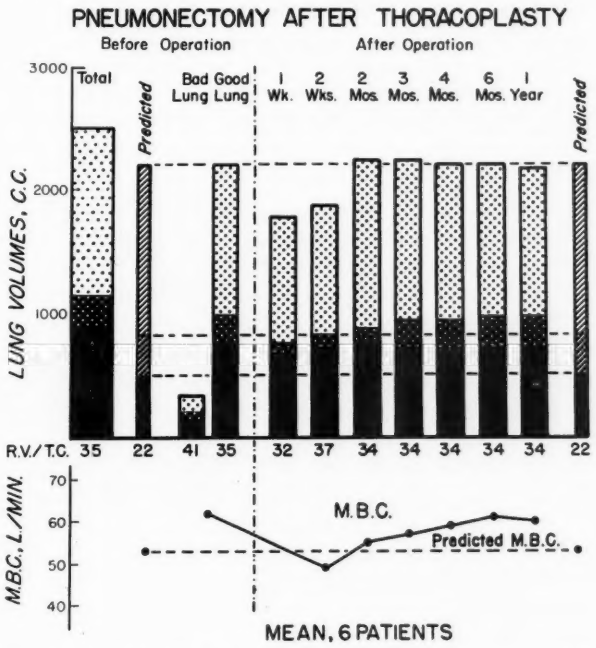

Fig. 15.—Mean function studies of six patients who had pneumonectomy after thoracoplasty failed.

Late thoracoplasty corrected overdistention at maximal inspiration chiefly at the expense of the vital capacity. It corrected overdistention on fullest expiration only partially. It caused a definite and permanent loss of maximum breathing capacity. These are striking findings since the thoracoplasty was done over an empty hemithorax. Possible causes for this will be discussed subsequently.

7. *Pneumonectomy After Thoracoplasty.*—The lung was removed in six patients after thoracoplasty had failed. Thoracoplasty had been performed from two to thirteen years prior to resection, and had been extensive (eight to ten ribs). Thoracoplasty failures with fewer ribs removed usually had secondary lobectomies.

Findings after this procedure, summarized in Fig. 15, can be stated briefly. Except for the immediate postoperative period, pneumonectomy after extensive thoracoplasty had no effect on the total capacity or MBC of the single remaining lung. There was no overdistention in full inspiration either before or after resection and there was a moderate overdistention in the pulmonary midposition both before and after. The functional residual capacity was increased and the residual volume occupied 35 per cent of the total capacity before operation and 34 per cent two months to one year after resection.

Thoracoplasty Versus Pneumonectomy for the Functionless Lung.—In the course of a detailed study of the ventilatory defect due to thoracoplasty, it was noted that this procedure caused a considerable permanent loss of function even if performed over an apparently functionless lung.[24] Ten patients were selected from this group whose bronchospirometry prior to operation showed less than 10 per cent of the total resting ventilation on the side to be operated. Seven of these patients had total atelectasis due to empyema or therapeutic pneumothorax. Three patients had cavernous disease involving the entire lung. Their individual MBC and upright VC before operation, two weeks after every one of three stages of thoracoplasty, and six months after thoracoplasty are shown in Fig. 15. Their mean MBC before operation was 71 liters per minute and six months later 56 liters, a permanent loss of 21 per cent of maximal ventilatory capacity. The mean VC was 2,350 c.c. before operation and 1,725 c.c. six months later, a 27 per cent loss of maximal stroke volume.

In the present series of patients, pneumonectomy was performed for "destroyed lung" in twelve instances. By bronchospirometry, nine patients showed less than 10 per cent of the total ventilation on the side to be operated. Two others showed no patency of the mainstem bronchus by bronchoscopy and no aerated lung on that side by roentgenogram. The last patient had ulcerative endobronchial disease with stricture of the mainstem bronchus. The MBC and upright VC of this group before operation, two weeks after operation, and every month thereafter for six months are also shown in Fig. 16. Their mean MBC was 58 liters per minute before operation and 57 liters per minute six months later, a loss of only 2 per cent. The mean VC at the same time intervals was 1,675 c.c. and 1,625 c.c., again a decrease of only 3 per cent.

Our clinical experience supported these data. There were several patients in the thoracoplasty group who were not dyspneic with one functioning lung before collapse and who had moderate dyspnea six months after thoracoplasty over a totally atelectatic lung. A number of these patients had total empyema of many years' duration with marked emphysema of the remaining lung. They often had considerable respiratory difficulty, and one such patient died of respiratory failure shortly after a first-stage thoracoplasty.

Several patients who had a nonfunctioning lung removed were moderately dyspneic before operation. One woman, before pneumonectomy, had an MBC of 32 liters per minute or 29 per cent of predicted and a VC of 820 cubic centimeters. Although she required oxygen inhalation therapy for about two weeks after resection, she was less dyspneic six months after the operation than before

resection. Her MBC at that time was 34 liters per minute and her VC 880 cubic centimeters. She has worked as a full-time secretary for the past two years.

The laboratory data and clinical experiences were further underlined by the lung volume and maximal function studies before and after thoracoplasty of a hemithorax from which the lung had been previously removed (Tables II and VII, Figs. 12 and 14). Almost invariably, this secondary procedure caused a further and permanent loss of maximal function. This was most strikingly demonstrated in the group who had thoracoplasty late after pneumonectomy, because the patients had had opportunity fully to recover from the resection (Fig. 14).

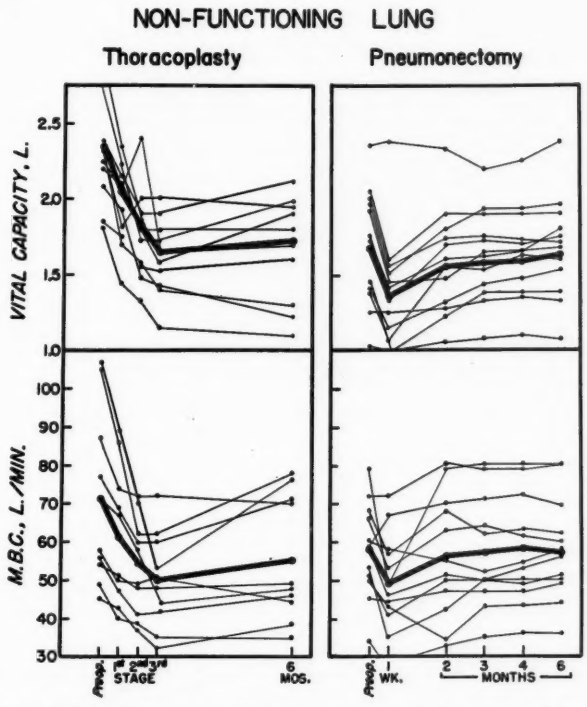

Fig. 16.—Serial maximum breathing capacity and vital capacity studies in patients who had primary thoracoplasty or primary pneumonectomy of lungs which showed less than ten per cent of the total function prior to operation.

It must be concluded that thoracoplasty over a functionless lung usually causes a permanent loss of function whereas resection of such a lung usually does not. It might be argued that the functional effectiveness of the diseased lung prior to collapse was underestimated for one reason or another. However, the studies of the effect of thoracoplasty of an empty hemithorax prove that destruction of an extensive portion of the hemithorax impairs the functional efficiency of the contralateral lung.

Two mechanisms, both originating with the postural changes due to thoracoplasty may be responsible for the loss of function. The proper functioning of the muscles of respiration depend in part on the application of symmetrical leverage. This is perhaps illustrated by the occasional spontaneous fracture of the first contralateral rib after a thoracoplasty in the course of which, the accessory muscles of respiration in the neck have been severed from their insertions to the ribs. When a contraction of some respiratory muscles is no longer counterbalanced by an equal contralateral contraction, their action becomes less efficient.

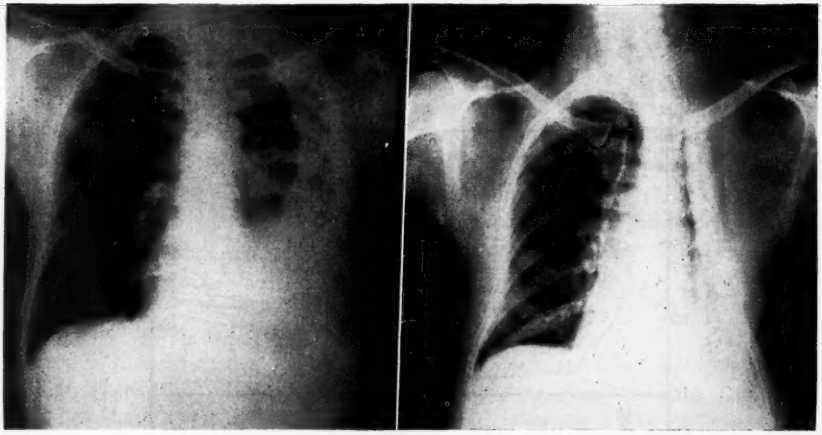

Fig. 17.—Roentgenograms of the chest of patient J. O'K. before and one year after a standard ten-rib thoracoplasty. The alteration of the size and shape of the contralateral hemithorax is illustrated.

The scoliosis is, in part, due to the unequal pull of the respiratory muscles, and, in part, to relaxation and interruption of the costospinal muscle groups. This scoliosis may be responsible for the second mechanism of functional reduction. The thoracic cage on the contralateral side becomes partly "jack-knifed." This not only reduces the functional residual volume of the remaining lung, but all other components of the lung volume as well (Fig. 14).

The maximal effort is impaired by less effectively functioning respiratory muscles and the stroke volume is reduced by "jack-knifing" of the rib cage. This is illustrated by the roentgenograms of Fig. 16. This patient was admitted with a left pyopneumothorax. Bronchospirometry showed no oxygen uptake and no respiratory excursions on that side. A two-stage, ten-rib thoracoplasty caused moderate scoliosis, a well-marked "jackknifing" of the contralateral thoracic cage (Fig. 17) and a loss of MBC of 30 per cent, which was not regained during the first year after operation.

In patients with marginal pulmonary function, thoracoplasty should be approached with caution even if there is no lung or a destroyed lung on the side to be collapsed.

CONCLUSIONS

There is no preponderance of evidence that chronic overdistention leads to true pulmonary emphysema with the histologic changes characterized by disruption of the pulmonary parenchymal architecture. Only one of the physiologic manifestations of emphysema, an increased ratio of residual volume to total lung capacity (RV/TC) was present in many patients who showed marked overdistention. Additional characteristics of emphysema, such as reduced timed vital capacity percentages, elevated intrapulmonary mixing indices, low immobile diaphragms, decreased arterial oxygen saturation, and increased arterial and alveolar carbon dioxide tension were all absent in patients who had not shown these changes prior to resection. The total predicted and determined vital capacities, together with the volumes expired during the first, first two,

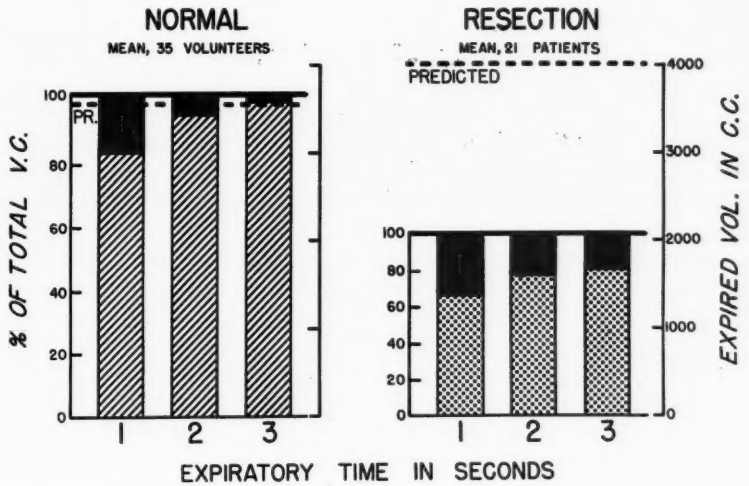

Fig. 18.—Predicted, total determined and timed vital capacities in normal volunteers and in patients with pneumonectomy without aftertreatment. The one-second, two-second, and three-second capacities were obtained with a modified vital capacity instrument and an electronic timer.

and first three seconds of the effort are shown for thirty-five normal volunteers and patients with pneumonectomy without aftertreatment (Fig. 18). Patients with one lung showed a severe restrictive ventilatory insufficiency. The stroke volume (VC) was reduced to almost one-half of the predicted for two lungs. However, there appeared to be a slight obstructive element also. Whereas normal volunteers were able to exhale 83, 94, and 97 per cent of their total vital capacity in the first, first two, and first three seconds of the effort, patients after pneumonectomy exhaled only 67, 77, and 79 per cent of their total vital capacity at the respective time intervals.[18] In only a few patients was there a slight progressive decrease of the MBC, two and two and one-half years after operation. In one patient, there was good evidence of rapid progression of pre-existing em-

physema. It is thought probable but not certain that pulmonary parenchymal disruption will eventualy be the end result of chronic overdistention.

Overdistention did not lead to true emphysema in young people after pneumonectomy within the first two and one-half years. In this respect, the study must be regarded as a preliminary report.

From the present investigation, it can be concluded that some overdistention of the remaining lung cannot be avoided if the empty hemithorax is not treated. It was shown that the extent of this overdistention is unpredictable and varies greatly from patient to patient. A prosthesis of oil, plastic sponge or air under slightly positive pressure obviated entirely overdistention of the remaining lung and mediastinal shift. Such prostheses caused no further loss of maximal ventilatory function. Thoracoplasty within three months after resection also prevented overdistention but did cause a definite additional loss of maximal ventilation. Thoracoplasty performed more than six months after resection caused only a partial return of the opposite lung to its normal confines, and also produced a very definite and permanent further loss of pulmonary function.

If it is accepted that overdistention is undesirable, then with prevention of overdistention as the only objective in mind, a clear choice of treatment following pneumonectomy can be made from information obtained in this study. Pneumothorax, later followed by plastic sponge plombage, offers the ideal answer to this objective.

However, prevention of overdistention should always be only one of many objectives all of which together can be summarized as the optimal well-being of the patient. The maintenance of a large air-filled dead space often exposed to tuberculous mediastinal lymph nodes and a bronchial stump with peribronchial and endobronchial disease should not be accepted as the procedure of choice without far greater experience and evaluation from the surgical viewpoint. Indeed, the authors strongly suspect that the incidence of empyema with this form of treatment is higher than with thoracoplasty or with no treatment.

Furthermore, the introduction of a plastic sponge, even though a relatively inert foreign body, is a surgically unattractive idea, particularly in young patients and in patients with tuberculosis.

At this time, we do not wish to be interpreted as advocating the use of these methods in patients in whom resection has been performed for tuberculosis except in very special circumstances. The observations made, however, can be transferred to the group of patients in whom resection is done for malignant tumors of the lung. In this group, pre-existing emphysema, marginal pulmonary function, a poor general condition, and a questionable prognosis all make supplementary thoracoplasty undesirable. These very conditions make prevention of overdistention highly important. Pneumothorax followed at a variable interval by introduction of a plastic sponge prosthesis or even primary plastic sponge plombage at the time of pneumonectomy may provide the ideal solution to this problem.

It is hoped that these data may serve as a base line for further studies directed at the conservation of pulmonary function and its maintenance at an optimal level following pneumonectomy.

SUMMARY

Forty patients were studied before pneumonectomy and at weekly and later monthly intervals thereafter, for six months to two and one-half years.

The techniques employed included standard pulmonary function studies, preoperative bronchospirometry, a modified method of residual volume determination permitting measurement of small changes in that value and a new method for determination of functional residual capacity and pulmonary mixing index for each lung separately before operation.

Pneumonectomy without aftertreatment was followed by a variable amount of overdistention. The severity of this overdistention could not be predicted before operation.

Maintenance of pneumothorax within the space after operation entirely prevented overdistention. This procedure was not accompanied by further reduction of maximal function.

Conversion of pneumothorax to oleothorax caused no alteration of pulmonary volumina or function.

Conversion of pneumothorax by a plastic sponge plombage prevented overdistention entirely and overdistention existing prior to pneumonectomy could be corrected by this procedure. Plombage was not accompanied by a further reduction of maximal ventilatory function.

Early thoracoplasty, six weeks to two months after resection, prevented overdistention on deep inspiration by reduction of the vital capacity but did not entirely prevent overdistention in the pulmonary midposition. This procedure caused a further loss of maximum breathing capacity.

Late thoracoplasty, six months to two years after resection, corrected existing overdistention only partially and caused a further, permanent reduction of vital capacity and maximum breathing capacity.

Pneumonectomy after unsuccessful, extensive thoracoplasty produced no change of pulmonary volumina or maximal ventilatory function.

Pulmonary function before and after primary pneumonectomy and primary thoracoplasty for functionless lungs were compared. It was shown that primary resection in these patients caused no further loss of function while the loss of function after thoracoplasty over functionless lungs was marked.

No definite indications were obtained that overdistention following pneumonectomy in young patients results in true emphysema with disruption of the pulmonary parenchymal architecture during the first two and one-half years after operation. Progression of true emphysema after pneumonectomy in the older patients was demonstrated.

The authors are indebted to Miss D. M. Donnelly and Miss S. S. Smith for their technical assistance.

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PULMONARY FUNCTION IN TRAUMATIC HEMOTHORAX TREATED BY DECORTICATION

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MANY members of this organization have participated in the valuable contributions relating to pulmonary decortication in the treatment of traumatic hemothorax.[1-13] The principles and practices evolved during the experience of World War II are the fundamentals of its present-day management. Recently, the Korean conflict has resulted in the concentration of a relatively large number of casualties suffering from thoracic injuries at Fitzsimons Army Hospital. Traumatic hemothorax was a concern of major significance, early treatment had been excellent, and one phase not previously studied was, within certain limitations, observed among these casualties. I refer specifically to pulmonary function studies in patients treated by decortication. The number of patients available in the early months of the campaign exceeded our facilities for functional studies, and many did not have pre- and postoperative functional evaluations. Exhaustive studies as described by Cournand and his associates, Wright, and others were not at the time feasible.[14-17] Data presented pertain only to certain preoperative and early postoperative functional findings. Factual observations will be detailed, certain interpretations will be suggested, but conclusions which these data may warrant will probably best be made by those with greater experience in this field of pulmonary dynamics.

MATERIAL

From among thirty-two casualties treated by pulmonary decortication for traumatic hemothorax during the period Sept. 26, 1950, to March 1, 1951, nineteen have had certain pulmonary function studies made including external spirometry and bronchospirometric determinations. This presentation is limited to the data obtained relative to the maximum breathing capacity noted by external spirometry and divided functional studies emphasizing oxygen consumption, vital capacity, and ventilation, as observed in these nineteen patients. All were young soldiers in physically good condition prior to their injury. Their ages varied from 18 to 31 years, and averaged 21 years. All were operated upon relatively early following injury, the time interval varying from thirty to ninety-seven days, and averaging sixty days. Two of the group had had prior open drainage for a frank empyema. In five (18 per cent) the presence of intrapulmonary foreign bodies were in themselves considered

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as warranting thoracotomy for their removal. Streptokinase and streptodornase were employed in several instances with favorable response in liquefying the intrapleural material. Bronchoscopy was normal in all instances, and no evidence of prior chronic pulmonary disease was observed. The functional studies were made from twenty-one to one hundred forty days postoperatively; the average for the group being sixty-one days. All were wounded in Korea, and all but one have returned to military duty.

CLINICAL CONSIDERATIONS

Probably the majority of patients suffering from the effects of traumatic hemothorax induced by the missiles of war present few problems in determining indications for decortication. In others the indications may be less definite. Our observations and military expediency influenced us to approach this problem with an appreciation that decisive action as to whether or not decortication should be recommended was necessary. Along with others we have repeatedly noted that decortication may be effectively accomplished months or even years after the initial injury. It was believed that the best functional results would be obtained if decortication was presently accomplished in this group of casualties, rather than to defer the decision for later evaluation. It is probable that certain of the patients in this series would have continued to carry on normal activities without any appreciable interference of pulmonary function had surgery not been performed. In several instances the functional disturbances were not marked, the adaptive functions of the body had made a favorable adjustment as far as clinical observations could ascertain, and whatever small or moderate improvement which might result from surgical intervention would in such instances not be impressive. However, we know of no reliable means by which the development of moderate or severe chronic pulmonary insufficiency may be forecast in these individuals.

Pulmonary function studies were undertaken as a probable aid in assessing factors influencing the indications for or against surgical intervention. These data were often unpredictable. Careful fluoroscopic evaluation of the motion of the lung and diaphragm was carried out in all patients pre- and postoperatively.

CASE 1.—A Filipino, aged 20 years, was wounded Nov. 1, 1950, in the left thigh. He was behind enemy lines and remained hidden in the hills until captured ten days later. After being held captive overnight, he was instructed to walk toward a ditch. Upon reaching the ditch, he was shot by enemy rifle fire in the left chest. The patient remained in the ditch until nightfall, apparently being left as dead by the enemy. After dark he emerged from the ditch and hid in uninhabited houses until he was discovered two days later by American forces. Thoracentesis of the left pleural space was carried out on four different occasions with unknown amounts of bloody fluid being removed. He was admitted to Fitzsimons Hospital on Dec. 18, 1950. Approximately four-fifths of the left lung field was opaque on roentgenographic examination. The left diaphragm was immobile, there was no foreign body present, and on December 27 pulmonary decortication removing a visceral and parietal peel varying from 0.5 to 1 cm. in thickness was accomplished. His maximum breathing capacity preoperatively was 20 liters. Eighty-four days postoperatively it was recorded as 64 liters. Bronchospirometric determinations relative to the left lung showed oxygen consumption of 20 per cent prior to operation and 29 per cent postoperatively. Vital capacity increased from

13 per cent to 27 per cent, and ventilation showed 20 per cent increase. His diaphragm moved well following operation (Figs. 1 to 3).

CASE 2.—This patient, aged 20 years, was wounded in the left chest on Aug. 20, 1950. Hemoptysis was moderate. Three thoracentesis with removal of 800 c.c. of bloody fluid was accomplished prior to admission to Fitzsimons Hospital on September 26. Repeated

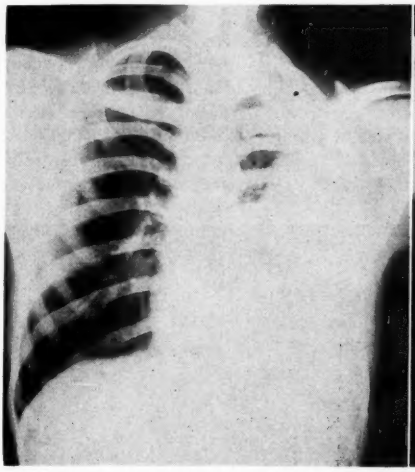

Fig. 1.

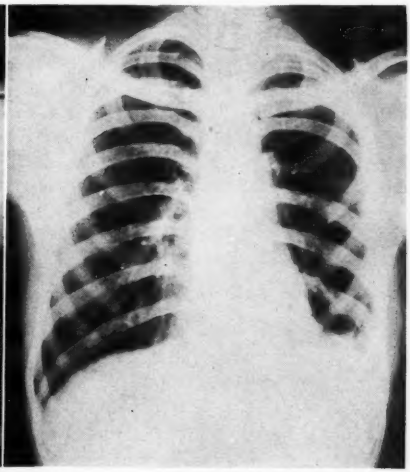

Fig. 2.

Fig. 1.—(Case 1) Traumatic hemothorax, left, seven weeks after initial injury.
Fig. 2.—(Case 1) Traumatic hemothorax, left, three weeks following decortication.

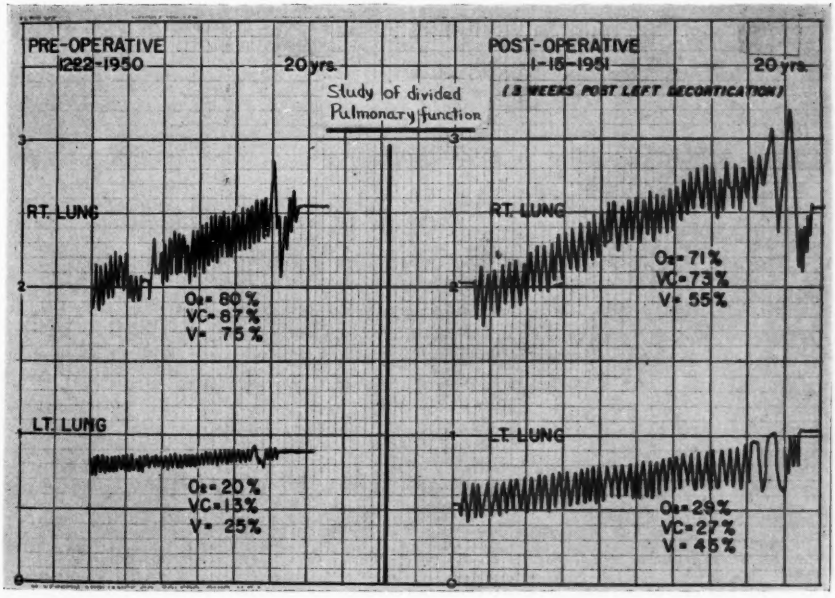

Fig. 3.—(Case 1) Bronchospirometric findings.

thoracentesis failed to accomplish re-expansion of the lung, and on October 23 pulmonary decortication was performed with the removal of two foreign bodies from the left lung. Maximum breathing capacity, preoperatively, was 68 liters, and seventy-seven days postoperatively it was recorded as 114 liters. Bronchospirometric determination relative to the left lung showed a gain of 9 per cent in oxygen consumption, a 7 per cent decrease in vital capacity and 3 per cent increase in ventilation on the seventy-seventh day postoperatively (Figs. 4 and 5).

CASE 3.—Aged 18, wounded September 2 in the right chest, the missile traversing the right lung, lodging in the left lung. Repeated thoracentesis with removal of unknown amounts of bloody fluid on the right was accomplished prior to admission to Fitzsimons Hospital September 24. The bilateral nature of injury with a known hemothorax on the right and two foreign bodies on the left presented a problem of evaluation as to surgical intervention. The right diaphragm was immobile and the left diaphragm moved sluggishly. Maximum breathing capacity preoperatively was 37 liters. Decortication of the left lung and

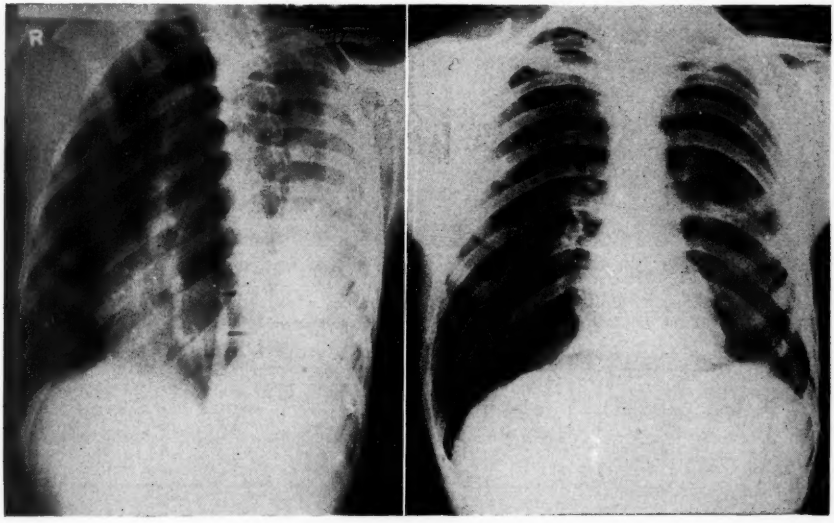

Fig. 4. Fig. 5.

Fig. 4.—(Case 2) Traumatic hemothorax, left, ten weeks after initial injury. Intrapulmonary foreign bodies, left.

Fig. 5.—(Case 2) Twelve weeks after decortication and removal of foreign bodies.

removal of foreign bodies were accomplished forty-seven days after injury, and twenty-eight days postoperatively functional studies revealed the following: maximum breathing capacity 72 liters, an increase of 35 liters over the preoperative determination. Oxygen consumption on the left was within normal limits preoperatively and decreased from 50 per cent to 47 per cent after operation. Vital capacity was 37 per cent prior to operation and increased 10 per cent after operation. Ventilation was 50 per cent preoperatively and decreased 6 per cent postoperatively.

Physiopathologic considerations resulting from a traumatic hemothorax due to the missiles of war have been thoroughly discussed elsewhere.[5, 6, 9] Simply stated as a working concept, it is our understanding that the pulmonary volume is reduced, and the encased or imprisoned lung is limited in participation in the act of breathing. The lung takes up less oxygen than it should, the pulmonary artery system responds by diminishing

the blood flow through the lung attempting to prevent hypoxia, and a nonexpansile "peel" or membrane is formed as a result of the organization of blood and fluid in the pleural space. The degree to which these factors operate is variable, but is generally conceded to be progressive. The removal of the plombage of organized blood and exudate and the nonexpansile membrane should, it is believed, offer the best opportunity for re-expansion of the lung and return to as nearly as possible normal function. We have not been impressed by the problems or the results obtained as whether or not the parietal peel is removed. The parietal portion of the peel is generally removed but in several instances this peel has appeared to be of no particular significance and no special effort has been made to accomplish its removal. The time required for the maximum return of the function of the previously encased lung was not ascertained in our study. It would be an interesting observation to be able to carry out further functional studies on these or similar patients at intervals of several months or years. It is hoped that this may, in certain instances, be accomplished.

MAXIMUM BREATHING CAPACITY

Maximum breathing capacity is considered to be a most effective measurement of the bellow action of the chest, a reasonably accurate measurement of the patient's potential response to exertional stress, and a preferable method of evaluating respiratory reserve. Maximum breathing capacity measures the maximum amount of air moved in and out of the lungs per unit of time. In the sixteen patients in whom this observation was made by external spirometry, ten showed an increase postoperatively averaging 21 liters, while five showed a decrease averaging 15 liters and in one patient there was no change. The most striking changes were in Cases 1 and 2. The data on all patients are listed in Table I.

TABLE I. MAXIMUM BREATHING CAPACITY

SIDE INJURED	PREOPERATIVE	POSTOPERATIVE	PERCENTAGE INCREASE CHANGE	PERCENTAGE DECREASE CHANGE
L	70	105.6	36	
R	75	80	5	
L	70	70	0	
R	79.2	70.4		9
R	80.8	83.6	3	
L	88.4	67.6		21
L (operated) (bilateral injury)	37	72	35	
L	117.6	92		26
L	20	64	44	
L	91.4	96	5	
L	87.4	80.6		7
R	83.6	72		12
L	68.2	114.4	46	
R	76	96.8	21	
R	66	76	10	
L	67.2	71.6	4	

BRONCHOSPIROMETRY

Bronchospirometry permits divided functional studies of each lung being made at the same time. The percentages of oxygen consumption, vital capacity, and ventilation were made for each lung graphically by the closed method. Gas samples were not analyzed for oxygen and carbon dioxide. The variations pre-and postoperatively were appreciable. These data are illus-

trated in Tables II, III, and IV. The most marked increases in these factors were noted in two patients in whom the maximum breathing capacity decreased 9 liters in one, and increased 4 liters in the other, as illustrated in the following case report.

TABLE II. BRONCHOSPIROMETRIC DETERMINATION (VENTILATION PERCENTAGES)

SIDE INJURED	PREOPERATIVE	POSTOPERATIVE	PERCENTAGE INCREASE CHANGE	PERCENTAGE DECREASE CHANGE
L	48.4	43		5
L	43	62	19	
R	44	50	6	
R	49.4	52	3	
L	50	52.5	3	
L	50	43.6		6
L	40	41.7	2	
L	37	54.5	18	
L	25	45	20	
R	46.5	56	10	
L	36.3	48	12	
L	44	39	5	
R	48.9	52.3	3	
L	39.6	42.9	3	
L	22	25	3	
R	40	48	8	
R	58	76	18	
L	29	40	11	

TABLE III. BRONCHOSPIROMETRIC DETERMINATION (OXYGEN CONSUMPTION PERCENTAGES)

SIDE INJURED	PREOPERATIVE	POSTOPERATIVE	PERCENTAGE INCREASE CHANGE	PERCENTAGE DECREASE CHANGE
L	37.5	58.4	21	
R	68.8	50		19
L	47	40		7
R	50	72.3	22	
R	41	51	10	
L	61	46.8		14
L (operated) (bilateral injury)	50	47		3
L	34	50	16	
L	30	32	2	
L	20	29	9	
R	37.5	53	16	
L	24	46	22	
L	23	44	21	
R	38	60	22	
L	23	32.6	10	
L	25	45	20	
R	40	54.6	15	
R	42.8	40		3
L	20	45.4	25	

CASE 4.—This patient, aged 18 years, was wounded in the right chest by a hand grenade Sept. 13, 1950, and was admitted to Fitzsimons Hospital on October 1. A metallic foreign body was present in the right lower lung field and the right diaphragm was moderately elevated and immobile. Decortication with removal of the foreign body was accomplished Oct. 15, 1950. The "peel" was most adherent and thickest, as is the usual situation, over the diaphragm laterally and posteriorly. The maximum breathing capacity preoperatively was 79.2

liters, and eighty-four days postoperatively was 70.4 liters. The oxygen consumption on the right preoperatively was recorded as 50 per cent and increased to 72 per cent postoperatively. Vital capacity showed a 12 per cent increase, and the ventilation was increased 6 per cent (Figs. 6 and 7).

CASE 5.—The patient, aged 24 years, was wounded in the left chest on Sept. 12, 1950. Several thoracenteses were performed with removal of an undetermined amount of blood prior to admission to Fitzsimons Hospital on October 2. Two foreign bodies were present in the

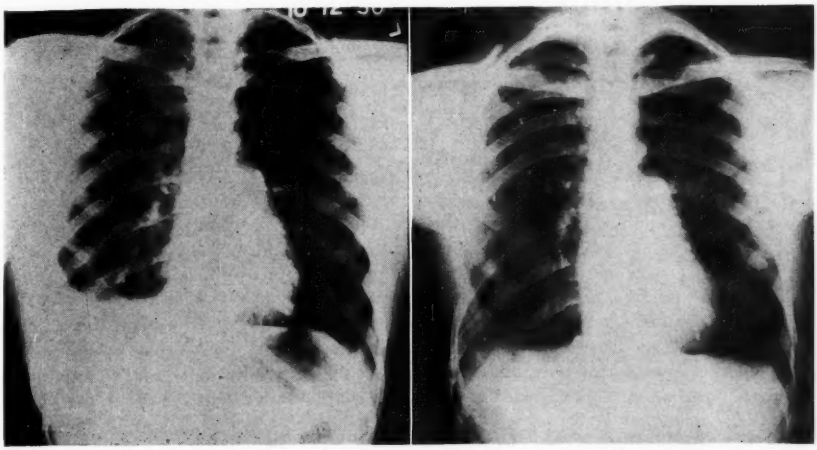

Fig. 6. Fig. 7.

Fig. 6.—(Case 4) Traumatic hemothorax, right, four weeks after initial injury.
Fig. 7.—(Case 4) Traumatic hemothorax, right, twelve weeks after decortication.

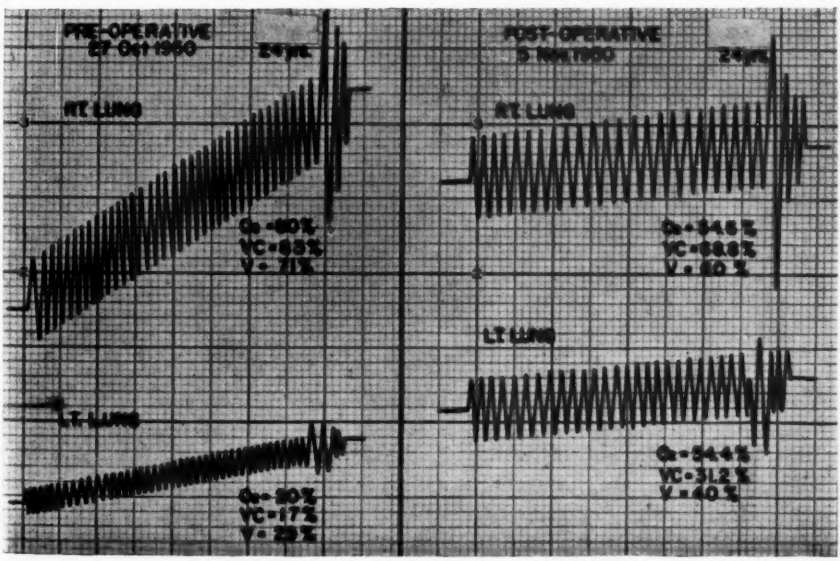

Fig. 8.—(Case 5) Graph of pulmonary function studies.

TABLE IV. BRONCHOSPIROMETRIC DETERMINATION
(VITAL CAPACITY PERCENTAGES)

SIDE INJURED	PREOPERATIVE	POSTOPERATIVE	PERCENTAGE INCREASE CHANGE	PERCENTAGE DECREASE CHANGE
L	31	37.5	7	
R	60	52		8
R	46	58	12	
R	45	45	0	
L	58	56		2
L	37	46.8	10	
L	28	28	0	
L	23	30	7	
L	13	37	24	
R	36.4	53	17	
L	43.3	30		13
R	41	53	12	
L	26.5	20		7
L	20	25	5	
R	35.2	37.5	2	
R	74.5	80	6	
L	17	31.2	14	

left lung, and the left diaphragm was elevated and fixed. Decortication and removal of one foreign body in the left lung was accomplished on Nov. 3, 1950. Bronchoscopy was negative. Pulmonary function determination thirty-four days postoperatively revealed an increase of four liters in the maximum breathing capacity. On the operated side the oxygen consumption increased 34 per cent, vital capacity 14 per cent, and ventilation 11 per cent (Fig. 8).

The correlation of the factors of oxygen, vital capacity, and ventilation pre- and postoperative is not attempted, but it is interesting to note that only two patients showed a decrease in ventilation postoperatively on the injured side, and this was slight (5 per cent and 6 per cent). This may be partially due to the fact that these patients had apparently normal lungs before injury, their youth, and that the lung was encased for a relatively short period. Re-expansion permits but it does not necessarily follow that ventilation will be increased, and the over-all percentage increase of the sixteen patients was only 9 per cent (Table II). Vital capacity increase averaging 11 per cent occurred on the operated side in eleven patients, while four showed a decrease of 8 per cent, and in two there was no change (Table IV). This may be due to the relatively early period after operation that the determinations were made, and further increase may develop later. Physiotherapy was a constant adjunct in therapy. The increase in oxygen consumption on the operated side averaged 17 per cent in fourteen patients, and a decrease averaging 9 per cent occurred in five patients (Table III).

SUMMARY

This presentation reports the findings pre- and postoperatively of certain pulmonary function tests in 19 unselected patients suffering from hemothorax due to war injuries and treated by pulmonary decortication. These determinations were made early following operation, averaging sixty days, and studies made after a longer postoperative interval might alter these findings. These observations indicate that the most uniform finding is an improvement in the

percentage of ventilation on the operated side, that oxygen consumption, vital capacity, and maximum breathing capacity show a trend toward restoration of normal function on the injured side, and finally that in individual instances the findings are often unpredictable.

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LATE CHANGES IN VENTILATORY FUNCTION FOLLOWING THORACOPLASTY

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SEVERAL patients have been observed in our follow-up clinic with excellent therapeutic results after thoracoplasty, but complaining of increasing respiratory distress. They all demonstrated evidence of a rotoscoliosis frequently with prominence of the seventh cervical transverse process. Since scoliosis usually is a progressive deformity, the present study was undertaken to determine the changes in ventilatory function which occurred, and to attempt to analyze some of the factors which led to these changes.

Cournand[1, 2] and his co-workers made a detailed study of the early changes in pulmonary function following thoracoplasty. They concluded that the reduction in maximum breathing capacity following a standard seven rib procedure as a rule was not greater than 15 per cent. Furthermore, they observed that when scoliosis developed, the maximum breathing capacity was further reduced. This resulted in an increased tendency to dyspnea on mild exercise. More recently Gaensler and Strieder[3] have published data indicating that the reduction in maximum breathing capacity six months after thoracoplasty was greater (about 35 per cent) in patients in whom the lung, to be collapsed later, contributed 40 per cent or more of the oxygen intake. No mention is made of the number of ribs resected.

The subjects for this investigation were a group of twenty-four patients who had undergone a thoracoplasty three to twenty-seven years before; eight had been studied preoperatively. The only criterion of selection was that sputum had become negative following operation and had remained so up to the time of study.

METHODS

The data were obtained on an outpatient basis on individuals who had been asked to omit breakfast and had been allowed to rest for about thirty minutes before the studies were begun. Vital capacity and maximum breathing capacity were measured on a Benedict-Roth spirometer with ventilometer attachment. Predicted values were calculated from the formulas of Baldwin, Cournand, and Richards.[4] A study of serial roentgenograms on each patient was also made, with particular attention to the presence and development of scoliosis, the length of the anterior segments of the second, third, and fourth ribs removed, and the excision of the transverse processes.

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TABLE I. EIGHT CASES STUDIED BEFORE AND AFTER THORACOPLASTY

CASE	YEARS POST-OPERATIVE	NO. OF RIBS	ANTERIOR SEGMENTS 2, 3, 4	TRANSVERSE PROCESS	SCOLIOSIS	VITAL CAPACITY IN LITERS				MAXIMUM BREATHING CAPACITY L./MIN.			
						PRED.	OBS.	% PRED.	% CHG.	PRED.	OBS.	% PRED.	% CHG.
RB	P	9	2, 3	yes	mod. sev.	2.90	1.58	55		100	67	67	67
	6 mo.					2.80	1.00	36	35	100	42	42	37
	3					2.70	1.08	40	33	100	47	47	30
RH	P	9	no	yes	slight	4.70	3.29	70		118	109	92	
	2					4.40	2.57	59	16	124	86	70	24
	9					4.20	2.76	65	7	119	84	72	22
FH	P	7	2, 3, 4	yes	severe	5.20	2.70	52		132	57	43	
	4 mo.					5.20	1.78	34	35	132	38	29	33
	6					5.20	1.75	33	37	132	25	26	40
CV	P	7	2	yes	slight	3.15	1.89	50		116	54	55	
	3 mo.					3.24	1.40	43	14	106	42	40	27
	11 mo.					3.24	1.60	49	2	106	51	48	13
	9					3.50	1.40	40	20	99	46	46	16
WC	P	7	no	no	none	4.60	3.38	74		123	95	78	
	2½					4.90	3.15	65	12	131	100	77	1
MR	P	7	no	none	none	4.20	2.89	69		124	70	56	
	7					4.20	2.95	70	0	124	57	46	18
	8					4.20	2.40	57	17	119	65	52	7
OM	P	3 lt.	no	yes	none	4.10	3.66	89		115	92	80	
	2 mo.					4.10	2.80	68	24	115	79	69	14
	5	5 rt.	no	no	none	4.20	2.80	67	24	111	88	80	0
	5 Lt., 2 mo. rt.					4.10	2.30	56	37	108	94	87	0
JR	P	3 rt. 5 lt.	no 2, 3	no	none none	4.88	2.46	51		111	62	56	
	3 mo.					4.88	2.48	51	0	111	57	51	9
	9					4.88	2.58	51	0	111	55	49	12

TABLE II. TWENTY-FOUR CASES STUDIED AFTER THORACOPLASTY

CASE	YEARS POSTOPERATIVE	NO. OF RIBS	ANTERIOR SEGMENTS 2, 3, 4	TRANSVERSE PROCESS	SCOLIOSIS	VITAL CAPACITY IN LITERS			MAXIMUM BREATHING CAPACITY L./M.		
						PRED.	OBS.	% PRED.	PRED.	OBS.	% PRED.
MK	15	11	2, 3, 4	no	severe	2.79	1.00	36	98	21	22
LB	21	11	2, 3, 4	no	moderate	3.68	1.80	45	95	40	42
GH	9	10	2, 3, 4	yes	severe	3.08	1.72	56	72.5	43	59
H	17	10	no	no	none	4.82	3.36	70	138	125	90
CL	8	9	2	yes	none	3.00	1.85	62	80	73	90
HE	5	9	2, 3, 4	yes	severe	3.18	1.10	34	77	59	75
RB	3	9	2, 3	yes	mod. sev.	2.70	1.08	40	100	47	47
RH	9	9	no	yes	slight	4.20	2.76	65	119	84	72
SP	27	9	no	no	none	2.82	2.56	90	81	81	100
TD	3	8	no	yes	none	3.90	2.70	70	104	49	47
FH	6	7	2, 3, 4	yes	severe	5.20	1.75	33	132	25	19
GN	3	7	2, 3, 4	yes	severe	4.30	2.25	52	104	45	43
CI	5	7	2, 3, 4	yes	mod. sev.	5.29	2.02	39	145	68	47
MI	5	7	2, 3, 4	no	mod. sev.	2.85	1.54	54	97	45	48
SD	3½	7	2, 3, 4	no	mod. sev.	3.70	1.90	50	115	58	50
SR	22	7	2, 3, 4	no	mod. sev.	4.40	2.20	50	123	78	63
CV	9	7	2	yes	slight	3.50	1.40	40	99	46	46
TA	5	7	no	no	diaphragm fixed	3.21	1.15	36	89.1	43	48
			no				2.40	57			
MR	7	7		no	none	4.20			119	65	52
WC	2½	7	no	no	none	4.90	3.15	65	131	100	77
KI	6	7	no	no	none	4.00	3.30	82	113	97	94
LM	6	7	no	no	none	3.25	2.21	69	84	84	100
JR	9	3 rt. 5 lt.	2, 3	no	none	4.88	2.58	51	111	55	49
OM	5	3 lt.									
	2 mo.	5 rt.	no	yes	none	4.10	2.30	56	108	94	87

RESULTS

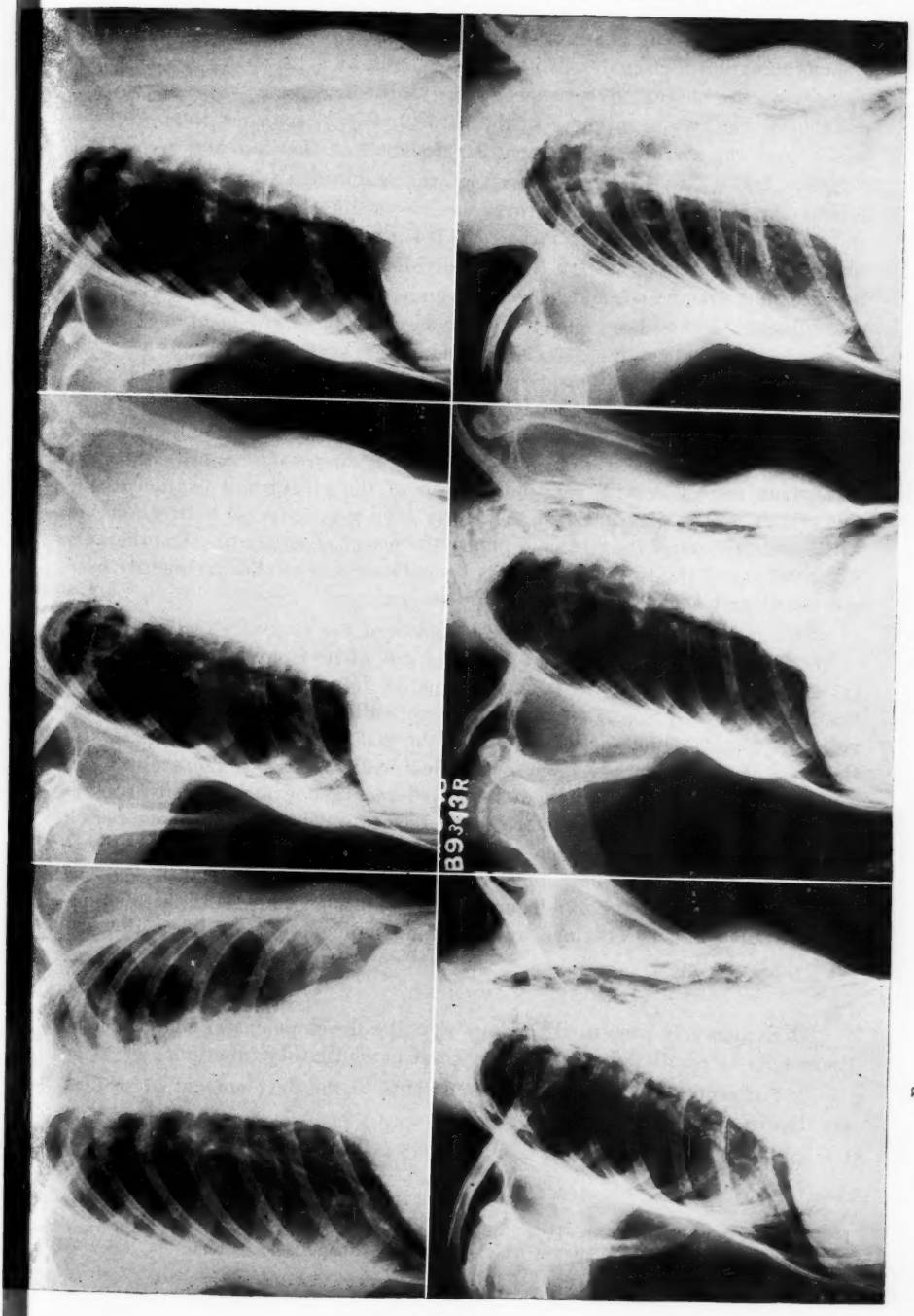
In the tables the cases have been grouped according to the number of ribs resected. Table I shows the results in those patients with preoperative and follow-up studies; Table II, the last postoperative result in each case. It will be seen that frequently the number of ribs resected was not the predominant factor in determining the functional result, and also the individuals' preoperative ventilatory function determined, to a large extent, the postoperative result. Of the twenty-four cases studied, eleven had at least a moderate degree of scoliosis. The maximum breathing capacity in this group averaged 46 per cent of predicted. In two patients studied pre- and postoperatively who developed scoliosis, the change in maximum breathing capacity was over 30 per cent. It also can be seen from the tables that the presence of scoliosis was invariably accompanied by a significant loss in ventilatory function. In addition, the removal of the first rib along with long anterior segments of the second, third, and fourth ribs and the transverse processes was usually associated with the appearance of the deformity. In those cases where one of these structures was left in place, the preservation of long anterior segments seemed most important in limiting the deformity. Although there were some patients without scoliosis in whom the functional result was poor, every case with good ventilatory function had a straight spinal column. It may be noted that when scoliosis did not develop there was slight improvement in late studies when compared to early postoperative figures.

The tables reveal a moderately high incidence of diminished ventilatory function. It is probable that the group with preoperative studies were frequently those in whom a diminished function was suspected, and hence this group is not a representative sample of patients undergoing thoracoplasty. It should be noted that the remainder of the patients in whom scoliosis is not present have figures which do not differ significantly from the predicted.

DISCUSSION

It has been pointed out that with the occurrence of scoliosis there is a considerable loss in function. This fact has been previously reported both in simple thoracoplasty[1, 2] and in thoracoplasty combined with pneumonectomy.[5, 6] Cournand and Berry[5] have reported a case after pneumonectomy (W. J.) in whom a progressive loss in ventilatory function due to overdistention was temporarily corrected by a thoracoplasty, but following the appearance of a severe, progressive scoliosis, much of the improvement was lost.

In most cases where long anterior segments of the second, third, and fourth ribs were removed, along with the transverse processes, a scoliosis of more than moderate degree resulted. Occasionally this was progressive over an extended period (Fig. 1). The occurrence of such a deformity when these structures were left in place was rare. Since there are many other factors which determine the functional result, the absence of a scoliosis does not insure good function. However, in every case where a significant degree of



D. E. F.

Fig. 1.—Serial roentgenograms over a nine-year period.

scoliosis did occur, the result from a functional standpoint was poor. A possible explanation for the deformity may be found by considering the muscular support of the thorax. There are four groups of muscles which act in opposition on the two hemithoraces; the paraspinals, the scalenes, the pectoralis minor, and the serratus. The complete removal of the first and second rib detaches the scalenes: the excision of the transverse processes, the paraspinals; and the removal of the long anterior segments of the second, third, and fourth ribs, the pectoralis minor. In freeing the scapula, the upper digitations of the serratus are often likewise divided. The muscles of the opposite side are now unopposed, and hence may undergo contracture with a resulting rotoscoliosis. It has been shown that if some of the above-mentioned structures are left in place, the deformity is much less severe. It appears that the most important structure in stabilizing the thorax is the long anterior rib segments. We have observed patients in whom all these structures were removed without scoliosis developing. Some of the factors which would tend to limit the appearance of deformity under these circumstances are: the presence of an empyema with resulting fibrosis of the pleura and fixation of the thoracic cage, the presence of a relatively long time interval between stages with reossification of the ribs, and finally the use of adequate physical therapy. The catching of the tip of the scapula beneath a lower rib has frequently been associated with severe and progressive scoliosis.

This report is not intended as a criticism of the over-all excellent results of thoracoplasty, but rather as a study of one of its complications. In some cases a radical procedure with its anticipated deformity and poor functional result may be the price of an adequate therapeutic result. Since, however, the majority of tuberculous lesions occur in the posterior and apical segments of the lung, it may seem advisable to do a less radical anterior thoracoplasty in these cases. The introduction of improved roentgenogram methods, such as lateral tomography, may, by more accurate localization of the lesions, permit a more limited operation which will still produce an adequate therapeutic result. In these lesions where their location requires the removal of long anterior segments to obtain an adequate collapse, it is possible that a better functional result could be obtained by combining pulmonary resection with a less radical thoracoplasty.

SUMMARY

1. Evidence is presented to show that the development of scoliosis after thoracoplasty resulted in a marked decrease in ventilatory function.

2. Some of the features which contribute to the development of scoliosis are discussed.

We wish to express our thanks to Dr. Andre Cournand for his helpful suggestions.

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LUNG FUNCTION STUDIES IN POUDRAGE TREATMENT OF RECURRENT SPONTANEOUS PNEUMOTHORAX

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IT IS now generally recognized that recurrent spontaneous pneumothorax of nontuberculous origin is best handled surgically. Several forms of treatment are available, but exploratory thoracotomy, resection of the pulmonary cysts, blebs, or bullae, with or without additional talcum powder poudrage to induce pleuritis, seems to be the preferred method of treatment. The use of talc to induce pleural symphysis has been criticized because of its supposed damage to lung function, and the purpose of this paper is to report on lung function studies in recurrent spontaneous pneumothorax treated by this method.

In the past a variety of irritating substances have been placed in the pleural cavity to cause pleuritis of sufficient degree to obliterate the pleural space. These substances have been inserted by needle, thoracoscope, or open thoracotomy. For example, Spengler, in 1906, utilized silver nitrate and later a solution of dextrose. Apostolides first used Guaicol and later suggested iodoform. Chandler preferred Gomerol. Iodized oil was introduced by Hennell and Steinberg, and iodized talc by Bethune and Medici.

The introduction of techniques of bronchospirometry made possible the study of individual lung function. The oxygen consumption and the ventilation of the individual lungs were found to be measurements of prime importance. The right lung being normally larger than the left utilizes from 52 to 56 per cent of the total oxygen consumed and does approximately the same proportion of the total ventilation. Pinner and his associates used bronchospirometric techniques in a series of patients and analyzed those cases in which a lung used less than 25 per cent of the total oxygen consumption. These authors found that most of their patients with markedly decreased lung function had pleural rather than parenchymal lesions. They stated, "Many lungs with active parenchymal lesions without pleural involvement show relatively little functional damage even if parenchymal lesions are extensive. It is of great practical importance that pleural involvement which cannot always be diagnosed by roentgenologic examination may lead to more serious functional damage than do much more obvious parenchymal lesions." Likewise, the statement has been made that pulmonary functional capacity is decreased in direct proportion to the severity of pleural symphysis, and that the production of a chemically induced severe pleuritis is inadvisable. Croxatto and Sampietro in a recent publication stated that minimal trauma to the pleura produced adhesions comparable in consistency to those produced by the instillation of irritating substances and supported their findings by pathologic sections.

Read at the Thirty-first Annual Meeting of The American Association for Thoracic Surgery, Atlantic City, N. J., April 16-18, 1951.

There have been thirty cases of recurrent spontaneous pneumothorax treated by exploratory thoracotomy and talc poudrage during the period 1943 to 1950 at Walter Reed Army Hospital and George Washington University Hospital. The great majority of these patients were in the military service at the time of the operation and all went back to military duty following operation. Long follow-ups have not been possible in all of these cases, but to our knowledge there have been no recurrences. Several of the patients were pilots and all returned to flying status after going back to duty. Four patients were chosen as representative of the group and underwent lung function studies before and after operation. Three of these had suffered repeated left-sided spontaneous pneumothoraces, and one had had several episodes of spontaneous pneumothorax on both the right and left side. Five operations were done on the four patients, and in all but one it was possible to excise the lesion suspected of being responsible for the production of the pneumothorax. This corresponds well with a report by Brewer, Dolley, and Evans in which the lesion was found in fourteen of fifteen of their own cases. These authors further reported that in a review of the literature the lesion was found in eighty-seven of ninety-five cases treated by thoracoscopy or thoracotomy. This would appear to indicate the advisability of exploration in these patients.

Prior to operation each of these patients was instructed in and became thoroughly familiar with Specific Remedial Breathing Exercise. The importance of these breathing exercises was emphasized to the utmost, and their active practice was begun early in the postoperative period. Beginning on the third postoperative day the patient reported to the Physical Medicine Clinic where a trained therapist guided them through exercise periods. The authors attribute much of the rapid complete return of good lung function to the diligent application of these exercises.

CASE REPORTS

CASE 1.—This patient was a 25-year-old white man admitted to Walter Reed Army Hospital following three proved episodes of left spontaneous pneumothorax over a two and one-half year period. A left exploratory thoracotomy revealed a small area of subpleural blebs at the apex of the left upper lobe which was excised. The left upper lobe was lightly powdered with sterile talc, and the chest closed with one posterior drain.

TABLE I

	BEFORE OPERATION			TWO MONTHS AFTER OPERATION		
	BOTH LUNGS	RIGHT LUNG	LEFT LUNG	BOTH LUNGS	RIGHT LUNG	LEFT LUNG
Complemental air	1200	1025	1155	1055	860	660
Tidal volume	590	525	265	1090	845	425
Supplemental air	1350	400	0	1056	245	240
Vital capacity	3140	1950	1420	3100	1950	1325
		58%	42%		60%	40%
Respiratory rate	15	18	18	19	17	17
Minute ventilation	10.4 L.	9.2 L.	4.8 L.	15.8 L.	11.3 L.	4.4 L.
		66%	34%		72%	28%
Oxygen consumption (c.c. per minutes)	192	155	125	430	220	220
% oxygen consumption		55%	45%		50%	50%

Pulmonary Function Data.—(See Table I.) Bronchospirometry before the operation showed that the right lung had a vital capacity of 1,950 c.c. (58 per cent of the total vital capacity), a minute ventilation of 9.2 liters per minute (66 per cent of the total minute ventilation), and an oxygen consumption of 55 per cent. The left lung had a vital capacity of 1,420 c.c. (42 per cent of the total vital capacity), a minute ventilation of 4.8 liters per minute (34 per cent of the total minute ventilation), and an oxygen consumption of 45 per cent.

Spirometry data obtained two months after the operation showed that the vital capacity had decreased from 3,140 c.c. to 3,100 c.c., or 80 per cent of normal. The minute ventilation and oxygen consumption were both increased. Bronchospirometry two months after operation showed that the right lung had a vital capacity of 1,950 c.c. (60 per cent of the total vital capacity), a minute ventilation of 11.3 liters per minute (72 per cent of the total minute ventilation), and an oxygen consumption of 50 per cent. The left lung was found to have a vital capacity of 1,325 c.c. (40 per cent of the total vital capacity), a minute ventilation of 4.4 liters per minute (28 per cent of the total minute ventilation), and an oxygen consumption of 50 per cent. These data show that the vital capacity fell from 3,140 c.c. before operation to 3,100 c.c. following operation. The relative vital capacities of the two lungs were unchanged by the operation. The relative minute ventilation of the left lung fell slightly after the operation from 34 per cent to 28 per cent. The per cent oxygen consumption of the two lungs was only slightly changed by the operation.

CASE 2.—The patient was a 23-year-old white man admitted to Walter Reed Army Hospital with a proved history of three left spontaneous pneumothoraces and five right spontaneous pneumothoraces over a period slightly in excess of six months. Left thoracotomy revealed subpleural blebs at the apex of the left upper lobe. After excision light poudrage was accomplished, and the chest closed with one drain. Two months later a right thoracotomy revealed blebs at the apex of the right upper lobe. These were also excised, the lung poudraged, and the chest closed with one drain.

TABLE II

	BEFORE OPERATION			TWO MONTHS AFTER LEFT OPERATION		AFTER BILATERAL OPERATION 4½ MONTHS AFTER LEFT SIDE 2½ MONTHS AFTER RIGHT SIDE		
	BOTH LUNGS	RIGHT LUNG	LEFT LUNG	RIGHT LUNG	LEFT LUNG	BOTH LUNGS	RIGHT LUNG	LEFT LUNG
Complemental air	1050	680	525	500	475	450	250	475
Tidal volume	700	820	450	1050	475	1500	1125	500
Supplemental air	1700	700	125	550	200	1050	375	225
Vital capacity	3450	2200	1100	2100	1150	3000	1750	1200
		67%	33%	65%	35%		60%	40%
Respiratory rate	10	9	9	10	10	13	21	21
Minute ventilation	8 L.	5.2 L.	2.8 L.	11.5 L.	4.5 L.	20 L.	20 L.	6 L.
		65%	35%	72%	28%		76%	24%
Oxygen consumption (c.c. per minute)	260	180	125	210	125	365	135	330
% oxygen consumption		59%	41%	63%	37%		29%	71%

Pulmonary Function Data.—(See Table II.) The pulmonary function data are summarized in Table II. Before operation the vital capacity was 3,450 c.c. The minute ventilation was 8 liters per minute. Bronchospirometry showed that the right lung had a vital capacity of 2,200 c.c. (67 per cent of the total vital capacity), a minute ventilation of 5.2 liters per minute (65 per cent of the total minute ventilation), and an oxygen consumption of 59 per cent. The left lung had a vital capacity of 1,100 c.c. (33 per cent of the total vital capacity), a minute ventilation of 2.8 liters per minute (35 per cent of the total minute ventilation), and an oxygen consumption of 41 per cent.

Approximately two months after the left-sided operation, bronchospirometry was again performed. At this time the right lung had a vital capacity of 2,100 c.c. (65 per cent of the total vital capacity), a minute ventilation of 11.5 liters per minute (72 per cent of the total minute ventilation), and an oxygen consumption of 63 per cent. The left lung had a vital capacity of 1,150 c.c. (35 per cent of the total vital capacity), a minute ventilation of 4.5 liters per minute (28 per cent of the total minute ventilation), and an oxygen consumption of 37 per cent. The data before and after the operation on the left side showed that the vital capacity on the two sides was unaffected by the poudrage procedure. The relative minute ventilation and the per cent oxygen consumption of the left side were slightly decreased.

Spirometry after the operation on the right side revealed a vital capacity of 3 liters (this was 87 per cent of the value before the first operation). The minute ventilation was 20 liters per minute. Bronchospirometry after the operation on the right side showed that the right lung had a vital capacity of 1,750 c.c. (60 per cent of the total vital capacity), a minute ventilation of 20 liters per minute (76 per cent of the total minute ventilation), and an oxygen consumption of 29 per cent. The left side had a vital capacity of 1,200 c.c. (40 per cent of the total vital capacity), a minute ventilation of 6 liters per minute (24 per cent of the total minute ventilation), and an oxygen consumption of 71 per cent.

From the data cited, it is apparent that poudrage on the left had relatively little affect upon the vital capacity. There was slight decrease in the minute ventilation on the left and a slight decrease in the per cent oxygen consumption on the left.

Four and one-half months after the left-sided operation, which was two and one-half months after the right-sided operation, the vital capacity was still 87 per cent of the value found before the first operation. The right and left lung vital capacities were not significantly changed by either poudrage. The minute ventilation of the right lung had increased from 65 per cent to 76 per cent of the total minute ventilation, whereas the per cent oxygen consumption of the right lung had risen from 59 per cent before the first operation to 63 per cent after the first operation, but then had fallen to 29 per cent after the second operation.

CASE 3.—The patient was a 21-year-old white man who had had three episodes of left spontaneous pneumothorax within three months. Left exploratory thoracotomy revealed tiny, subpleural blebs covering the entire lung surface. No leakage was apparent at operation, and no excision was carried out. The entire left lung was lightly powdered and the chest closed with drainage.

TABLE III

	BEFORE OPERATION			THREE MONTHS AFTER OPERATION		
	BOTH LUNGS	RIGHT LUNG	LEFT LUNG	BOTH LUNGS	RIGHT LUNG	LEFT LUNG
Complemental air		625	340	875	510	370
Tidal volume		520	240	650	300	240
Supplemental air		280	170	825	340	240
Vital capacity	2700	1425	750	2350	1150	850
		66%	34%		58%	42%
Respiratory rate		16	16	23	30	30
Minute ventilation		4.5 L.	1.8 L.	16.7 L.	8.4 L.	4.6 L.
		71%	29%		65%	35%
Oxygen consumption (c.c. per minute)		365	65	208	175	140
% oxygen consumption		85%	15%		56%	44%

Pulmonary Function Data.—(See Table III). Before operation this patient's vital capacity was 2,700 cubic centimeters. Bronchospirometry revealed that the vital capacity of the right lung was 1,425 c.c. (66 per cent of the total vital capacity), the minute ventilation was 4.5 liters per minute (71 per cent of the total minute ventilation), and the oxygen consumption was 85 per cent. The vital capacity of the left lung was 750 c.c. (34 per cent

of the total vital capacity), the minute ventilation was 1.8 liters per minute (29 per cent of the total minute ventilation), and the oxygen consumption was 15 per cent.

Spirometry approximately four months after the operation on the left side showed that the vital capacity was 2,350 c.c., and the minute ventilation was 16.7 liters per minute. Bronchospirometry nearly three months after the operation showed that the right lung had a vital capacity of 1,150 c.c. (58 per cent of the total vital capacity), the minute ventilation was 8.4 liters per minute (65 per cent of the total minute ventilation), and the oxygen consumption was 56 per cent. The left lung had a vital capacity of 850 c.c. (42 per cent of the total vital capacity), a minute ventilation of 4.6 liters per minute (35 per cent of the total minute ventilation), and an oxygen consumption of 44 per cent.

The left poudrage had little effect upon the total vital capacity but tended to increase the vital capacity of the left side. The minute ventilations of the two sides were not significantly changed, but again the left side showed a relative increase. However, the per cent oxygen consumption of the left side showed a distinct increase from 15 per cent before the operation to 44 per cent after the operation.

CASE 4.—The patient was a 20-year-old white man who suffered a right spontaneous pneumothorax one and one-half years prior to admission without recurrence. During that period three left spontaneous pneumothoraces occurred. At left thoracotomy apical subpleural blebs were seen and excised. The left upper lobe was lightly powdered and the chest was closed with drainage.

TABLE IV.

	BEFORE OPERATION			TWO MONTHS AFTER OPERATION		
	BOTH LUNGS	RIGHT LUNG	LEFT LUNG	BOTH LUNGS	RIGHT LUNG	LEFT LUNG
Complemental air		1150	1000	1585	1280	935
Tidal volume		400	100	1325	340	245
Supplemental air		250	0	1400	480	245
Vital capacity	4400	1800	1100	4290	2100	1325
		62%	38%		61%	39%
Respiratory rate		28	28	17	26	26
Minute ventilation		8.5 L.	1.4 L.	18.8 L.	6 L.	3 L.
		86%	14%		67%	33%
Oxygen consumption (c.c. per minute)		365	135	360	350	130
% oxygen consumption		73%	27%		73%	27%

Pulmonary Function Data.—(See Table IV.) This patient's vital capacity before operation was 4,400 c.c. Bronchospirometry before operation showed that the right lung had a vital capacity of 1,800 c.c. (62 per cent of the total vital capacity), a minute ventilation of 8.5 liters per minute (86 per cent of the total minute ventilation), and an oxygen consumption of 73 per cent. The left lung was found to have a vital capacity of 1,100 c.c. (38 per cent of the total vital capacity), a minute ventilation of 1.4 liters per minute (14 per cent of the total minute ventilation), and an oxygen consumption of 27 per cent.

Two months after operation spirometry data revealed that the vital capacity was 4,290 c.c. Bronchospirometry two months after operation revealed that the right lung had a vital capacity of 2,100 c.c. (61 per cent of the total vital capacity), a minute ventilation of 6 liters per minute (67 per cent of the total minute ventilation), and an oxygen consumption of 73 per cent. The left lung was found to have a vital capacity of 1,325 c.c. (39 per cent of the total vital capacity), a minute ventilation of 3 liters per minute (33 per cent of the total minute ventilation), and an oxygen consumption of 27 per cent.

These data show that the operation caused a 3 per cent decrease in vital capacity from 4,400 c.c. to 4,290 c.c. The relative vital capacities of the right and left lung were unchanged. The relative minute ventilation of the left lung increased from 14 per cent before the operation to 33 per cent after the operation. The per cent oxygen consumption of the two lungs was unchanged by the operation.

TABLE V. SUMMARY OF PULMONARY FUNCTION CHANGES CAUSED BY POUDRAGED

	VITAL CAPACITY BOTH LUNGS	% VITAL CAPACITY		% MINUTE VENTILATION		% OXYGEN CONSUMPTION	
		RIGHT	LEFT	RIGHT	LEFT	RIGHT	LEFT
Patient 1	3% ↓	2% ↑	2% ↓	6% ↑	6% ↓	5% ↓	5% ↑
Patient 2		2% ↓	2% ↑	7% ↑	7% ↓	4% ↑	4% ↓
	13% ↓ Bilateral operation	7% ↓	7% ↑	11% ↑	11% ↓	30% ↓	30% ↑
Patient 3	13% ↓	8% ↓	8% ↑	6% ↓	6% ↑	29% ↓	29% ↑
Patient 4	3% ↓	1% ↓	1% ↑	19% ↓	19% ↑	N.C.	N.C.

SUMMARY

Thirty patients have undergone exploratory thoracotomy and talcum powder poudrage in the treatment of recurrent spontaneous pneumothorax. Pulmonary function studies were accomplished on four patients, one of whom had surgery performed on both sides.

In Case 1 the vital capacity fell 3 per cent after the poudrage. The relative vital capacity of the left lung fell 2 per cent, the relative minute ventilation of the left lung fell 6 per cent, and the per cent oxygen consumption of the left side rose 5 per cent. These changes do not seem significant.

In Case 2 the vital capacity fell 13 per cent after the bilateral operation. After the left operation alone, the relative vital capacity of the left lung rose 2 per cent, the relative minute ventilation of the left lung fell 7 per cent, and the per cent oxygen consumption of the left side fell 4 per cent. None of these changes seem to be significant. After the second operation on the right side, the relative vital capacity of the right lung fell 7 per cent, the relative minute ventilation of the right lung rose 11 per cent, and the per cent oxygen consumption of the right side fell 30 per cent. The fall in per cent oxygen consumption on the right side after the right poudrage seems significant.

In Case 3 the vital capacity fell 13 per cent after the poudrage. The relative vital capacity of the left lung rose 8 per cent, the relative minute ventilation of the left lung rose 6 per cent, and the per cent oxygen consumption of the left side rose 29 per cent. This increase in oxygen consumption on the left side seems to be significant.

In Case 4 the vital capacity fell 3 per cent after the poudrage. The relative vital capacity of the left lung rose 1 per cent, the relative minute ventilation of the left lung rose 19 per cent, and the per cent oxygen consumption of the left side was unchanged. This increase in minute ventilation on the left side seems significant.

CONCLUSIONS

Open thoracotomy and talcum powder poudrage for recurrent spontaneous pneumothorax produced no consistent decrease in pulmonary function as determined by bronchospirometry in four patients. The observed changes in pulmonary function do not seem to be of greater degree than would be expected to follow any open thoracotomy. We conclude that the introduction of talcum powder to induce pleural symphysis has no demonstrable harmful effects during the period of our observation.

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DISCUSSION ON "PROGRESSIVE CHANGES OF PULMONARY FUNCTION AFTER PNEUMONECTOMY: THE INFLUENCE OF THORACOPLASTY, PNEUMOTHORAX, OLEOTHORAX, AND PLASTIC SPONGE PLOMBAGE ON THE SIDE OF THE PNEUMONECTOMY," BY DR. EDWARD A. GAENSLER, AND DR. JOHN W. STREIDER; "PULMONARY FUNCTION IN TRAUMATIC HEMOTHORAX TREATED BY DECORTICATION," BY DR. JAMES H. FORSEE AND MAJOR STEPHAN L. KYLAR; "LATE CHANGES IN VENTILATORY FUNCTION FOLLOWING THORACOPLASTY," BY DR. S. R. POWERS, JR., AND A. HIMMELSTEIN; AND "LUNG FUNCTION STUDIES IN POUDRAGE TREATMENT OF RECURRENT SPONTANEOUS PNEUMOTHORAX," LT. COLONEL JOHN PAUL, DR. EDWARD J. BEATTIE, JR., AND DR. BRIAN BLADES.

DR. FELIX A. HUGHES, Jr., Memphis.—I should like to discuss the paper on idiopathic spontaneous pneumothorax. We have had fifty-nine patients with spontaneous pneumothorax, amounting to 3.1 per cent of admissions to the thoracic surgery section at Kennedy Hospital. Observation and aspiration were sufficient treatments in twelve cases with small or minimal collapse. Major thoracotomy was used in five patients, because of large bullae in four patients and a clotted hemothorax in one.

Forty-two patients have been treated by closed drainage, using a Foley catheter with satisfactory results in forty of the forty-two. Expansion was prevented by a membrane over the lung of one patient. Although the lung expanded, large bullae required removal in the other case. Recurrence of pneumothorax occurred in three of the forty cases in which we had satisfactory results, and the lung re-expanded with the use of aspiration or drainage.

If poudrage will prevent recurrence, if it will allow maximum pulmonary function, if it is free of danger as a foreign body, its use might be advocated. I think if poudrage is not used the dangers of aspiration and of rapid expansion of the lung have been greatly exaggerated. Timidity and masterful inactivity are usually out of place in the treatment of spontaneous pneumothorax.

I would like to stress two points: First, closed drainage should usually be initiated early since re-expansion is often obtained in a matter of twenty minutes, even when the patient has been treated conservatively for months. Closed drainage is a ward procedure and offers little more discomfort than a thoracentesis. There is no immobility of the patient, since he can move around with a bottle or flask attached for drainage.

(Slides.) This patient had a pneumothorax and was treated conservatively for five months.

(Slide.) This shows the patient as he was discharged five days later.

The second thing I would like to stress is the use of a Foley or balloon catheter.

(Slide.) With the balloon inflated, the catheter tip can be held safely close to the chest wall. A catheter inserted 12 inches or more with the tip under thick fluid or fibrin cannot be expected to cause the lung to expand satisfactorily.

(Slide.) This shows adhesions and an air pocket at the site of the balloon and also a slight pneumothorax. It might be better to deflate the balloon a few hours before the catheter is removed.

This type of treatment of spontaneous pneumothorax has given satisfactory results in a high percentage of cases within a very short time.

DR. EARLE B. KAY, Cleveland.—I would like to discuss the paper by Dr. Gaensler and Dr. Strieder relative to postoperative pulmonary distention. The objective of pulmonary surgery is the removal of diseased tissue and the preservation of function of the residual lung. It was noted with concern that a certain number of patients developed basilar distention in the residual lobe following a previous lobectomy to an unfavorable degree in order to occupy the space previously occupied by the resected lobe. In an effort to determine the fate of the residual lobe following previous lobectomy function studies, bronchospirometric determinations, roentgenograms, and bronchograms were performed on a group of thirty-three postoperative patients followed from seven to seventy-three months, with an average of forty-one months. The pulmonary function studies were performed by Drs. Haven Perkins and Philip Crastnopol in the Respiratory Laboratory at Crile and Brecksville Veterans Hospitals. From these studies it was of interest to note the apparent value derived from performing a temporary phrenic neuremphraxis early in the postoperative period as a space reducing procedure. The patients not having phrenic operations (twenty-one) were compared to those who had the procedure (twelve).

(Slide.) Of twenty-one patients who did not have phrenic operations, thirteen (62 per cent) had either no or only minimal basilar distention. Eight of the patients (38 per cent) had moderate basilar distention. In contrast, in eleven of the twelve patients having associated phrenic operations, or 92 per cent, there was either only minimal (three cases) or no evidence of basilar distention (eight cases).

(Slide.) The ability of the residual lobe on the operated side to ventilate was much better in the phrenic group (75 per cent had normal ventilation) as compared to the nonphrenic group (33 per cent with normal ventilation).

(Slide.) The oxygen consumption in the nonphrenic group was below normal in 66 per cent of the patients, and in the phrenic group in only 26 per cent of the patients.

(Slide.) The ventilatory equivalent was within normal limits in 24 per cent of the patients without phrenics on the operated side as compared to 58 per cent within normal limits of those with phrenics.

From these studies it was felt that a temporary phrenic neuremphraxis performed early in the postlobectomy period was of value in preserving pulmonary function.

DR. G. W. WRIGHT, Saranac Lake, N. Y.—I would like to comment on three of the four papers. In regard to Dr. Gaensler's paper, I think we will all agree that to subject a patient to a space-correcting operation is a fairly serious procedure, and one should take

every pains to attempt to justify this action. The question of what overdistention means seems to me to be very important. For the majority of any twenty-four hour period of the day we do not go around with our lungs in a state of full expiration which is the size of the lung with residual air in it. Nor do we go around with our lungs maximally full, which is the size of the lung expressed by the total volume. Actually, for the majority of the twenty-four hour day the functional residual air determines the size or state of distention of the lung. In looking at Dr. Gaensler's data, it is perfectly obvious that the functional residual air is enlarged to some extent after resection without subsequent thoracoplasty or plombage. The important feature to me, however, is—what is the degree of this enlargement—and I would presume from looking at his data that it was of the order of a 15 to 20 per cent increase, some 300 c.c. which in terms of actual stretch of the lung causes only about 1 or 2 cm. of water change in the intrapleural pressure. In other words, I have the feeling that from his data the degree of distention is not very great from the actual physical point of view. Certainly it is not as great as happens in all of us when we change from the recumbent position to the standing position. As you know the functional residual air is increased by from 50 to 100 per cent in the normal man by a change from the recumbent to the standing position.

In view of the very slight effect of pneumonectomy on maximum breathing capacity, I think one should question whether or not there is clear-cut physiologic evidence to warrant doing a space-correcting operation after lobectomy, and perhaps even after pneumonectomy. I would like to ask Dr. Gaensler whether or not he believes his data indicate that the doing of a space-correcting operation is warranted on a functional basis in people after pneumonectomy.

In regard to the interesting patient reported by Dr. Forsee, I would like to point out that it is one thing to talk about pleural damage influencing lung function when the damage is caused by empyema; it is quite another when one speaks only of pleural synthesis. It is well known that pleural synthesis does not influence appreciably pulmonary function; for example all birds and certain mammals have no pleural space—the elephant has no pleural space. These animals do very well, and many human beings do very well with synthesis of the pleura. Therefore I would think that if a simple synthesis of the pleura may be accomplished, it would be a very useful thing in recurrent spontaneous pneumothorax.

Dr. Powers' paper interested me a great deal because we have wondered about this scoliosis. I did not quite clearly perceive how he distinguished between the functional effects of thoracoplasty per se; that is collapse of lung, and the effects of the torsion due to scoliosis.

DR. STRIEDER (closing).—With regard to Dr. Wright's remarks concerning the indications for a space-correcting procedure following pneumonectomy, I have nothing to say from a physiologic point of view beyond this: Dr. Gaensler's data would seem to indicate to us that there is justification for the procedure. Only summary data were shown on the slides, but details will appear in the published paper. It should then be evident that extreme overdistention may occur early or late, and there is no way of predicting when it will occur in a given case. With this in mind, we believe that means should be taken relatively early to prevent this, since such measures taken late are not so effective.

However, again, as was indicated in Dr. Gaensler's introduction, it is not only on the basis of physiologic data, without wishing to evade the issue that Dr. Wright raises, but there are also clinical facts that lead us under certain circumstances to correct the defect which has arisen as a result of pneumonectomy in a given patient. In this connection I refer to the fact that a patient may be uncomfortable purely on the basis of the mediastinal shift or tracheal deviation, in addition to what appears to us to be clinical evidence of overdistention, namely, that the patient is unhappy and dyspneic on exertion and has ineffectual cough.

DR. HIMMELSTEIN (closing).—Dr. Blalock, may I make one comment about the patient presented by Lt. Colonel Paul before I close?

We have been impressed by the development of talc granuloma in some of the abdominal surgery we have done and have not liked it. In treating recurrent spontaneous pneumothorax, we follow Mr. Brock's procedure, using one-half cubic centimeter of 10 per cent silver nitrate.

The comment is the fact that in these patients at six months we have tried to induce a pneumothorax by the technique usually employed in six or seven spots around the chest, and in six of the seven patients have been unable to find a pneumothorax space.

In closing our paper I would like to answer Dr. Wright's question. We have not specifically listed the effects of thoracoplasty, but merely have pointed out that we have obtained our best results when the spine is straight, and that when scoliosis did occur it usually was accompanied by about 50 per cent or greater reduction in maximum breathing capacity, which is an effect one would not anticipate just from the thoracoplasty.

LT. COLONEL PAUL (closing).—I wish to thank the discussors of the paper. In answer to Dr. Hughes' question concerning chronic pneumothorax, I would state that the present series of cases contained no cases of chronic pneumothorax but was confined to the treatment of recurrent spontaneous pneumothorax. All the patients had experienced at least three episodes of spontaneous pneumothorax of nontuberculous origin. In the military service the problem exists as to whether a man is fit or unfit for full military duty. We have found that thoracotomy with poudrage is a very effective method of handling recurrent spontaneous pneumothorax enabling us to return these patients to a full duty status after a minimum of hospitalization.

THE SIGNIFICANCE OF CELL TYPES IN BRONCHOGENIC CARCINOMA*

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BRONCHOGENIC carcinoma is no longer a disease seen as a curiosity clinically and at necropsy. It is a disease which, if seen early enough, can be eradicated surgically. It is important, therefore, to establish morphologic criteria by which one can determine to some degree operability and chances of survival after resection. Grading bronchogenic carcinoma furnishes little of value surgically or prognostically.

Bronchogenic carcinoma is a primary carcinoma of the lung, of varied histologic types, apparently arising from the surface mucosa of the bronchi or bronchioles. The mucous and serous glands of the bronchial wall are believed to be the site of origin of an entirely different type of tumor, namely, those of the adenoma and cylindroma group. The biologic behavior of tumors of the last-mentioned group is sufficiently unlike that of bronchogenic carcinoma to warrant their exclusion. The definitive diagnosis of bronchogenic carcinoma is not always possible from the examination of a resected specimen, particularly in peripherally placed tumors, because of the simulation of bronchogenic carcinoma and metastatic carcinoma.

In studies to be reported on in the following four papers adenomas and cylindromas were eliminated on the basis of histologic examination of the tumor. In order to exclude metastatic carcinoma, any patient who had a primary carcinoma, elsewhere was excluded from the study.

The histopathologic portion of these studies was made separately from the clinical portion. When the pathologic studies were completed, the clinical, surgical, and cytologic aspects of the various cases were correlated with the various histopathologic groups. The following four papers present the results.

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*Editor: This is an introductory statement to precede four papers: one by McBurney and co-workers, one by Carlisle and co-workers, and two by Patton and co-workers.

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BRONCHOGENIC SMALL-CELL CARCINOMA*

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THERE have been many studies of bronchogenic carcinoma, but infrequent ones of individual cell types. Our study is concerned with a clinical and pathologic study of small-cell bronchogenic carcinomas seen at the Mayo Clinic.

METHODS AND MATERIAL

The records and tissue of all cases of tumor of the lung encountered at the clinic through 1948, on which pathologic material was available for study, were reviewed. No cases were included in which the diagnosis was made on a clinical basis only. This involved study of biopsy and cytologic material in 1,153 cases.

It was deemed necessary to restudy all tissue, because in past years the pathologic diagnosis of bronchogenic carcinoma was not broken down according to cell types, and also because we wished to be certain that adenomas or other misdiagnosed lesions were not included. Cases in which there was a roentgenographic shadow in the lung and in which positive results were obtained on biopsy of the cervical nodes were not included because it was felt that this evidence, while suggestive, was not conclusive for carcinoma of the lung.

New sections were cut and stained with hematoxylin and eosin in instances in which the routine slides were unsatisfactory for study. The lungs in all cases in which resection was done were also studied.

Following the study of the microscopic sections the clinical records were then reviewed and follow-up studies done.

CLINICAL DATA

Of the 1,153 cases, 849 were felt to represent primary bronchogenic carcinoma. Of this number, in seventy-five (8.8 per cent) the diagnosis was small-cell bronchogenic carcinoma. An additional fifteen cases were included in the study on the basis of positive cytologic evidence alone.

Ninety per cent of the cases fell into the age group 40 to 69 years (Table I). The youngest patient was 30 years old, while the oldest was 75 years of age.

There were 87 males and 3 females, or a ratio of 29 to 1. Eighty-one of the patients were Anglo-Saxon or Scandinavian, seven Jewish, one Mexican, and one Spanish.

Data on the use of tobacco were not complete enough to be significant. As might be expected, most of the patients were smokers to some degree.

Occupation did not seem to be a significant factor, as there were many occupations represented.

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*Abridgement of thesis submitted by Dr. McBurney to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Surgery.

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TABLE I. AGE DISTRIBUTION IN 90 CASES OF SMALL-CELL BRONCHOGENIC CARCINOMA

AGE, YEARS	CASES	PER CENT
30-39	7	7.8
40-49	20	22.2
50-59	43	47.8
60-69	18	20.0
70 or more	2	2.2
Total	90	100.0

Symptoms and Physical Signs.—The average duration of symptoms was 5.9 months; however, in forty-nine cases the duration was less than four months, with about one-fourth of the patients having symptoms of less than two months' duration (Table II).

TABLE II. DURATION OF SYMPTOMS IN 88 CASES OF SMALL-CELL BRONCHOGENIC CARCINOMA*

DURATION (MONTHS)	CASES	DURATION (MONTHS)	CASES
Less than 1	5	6	3
		7	6
1	20	8	2
2	17	9	3
3	7	10-11	11
4	2	12-23	4
5	5	24	3

*Duration unknown in one additional case. Story unreliable but possibly of three-year duration in one additional case.

The symptoms were identical with those of any group of carcinomas of the lung in general. Table III indicates the early and most prominent symptoms in the cases.

The signs elicited were again those of bronchogenic carcinoma in general. The most significant and striking ones are listed in Table IV. It is of interest that almost 10 per cent of patients had very little evidence of thoracic disease on physical examination.

TABLE III. EARLY SYMPTOMS IN 90 CASES OF SMALL-CELL BRONCHOGENIC CARCINOMA

SYMPTOM	CASES	SYMPTOM	CASES
Cough	58*	Fever	7
Pain in chest	27*	Weakness	6
Dyspnea	16	Vomiting	2
Episodes of pneumonia, influenza or chest colds	15	Anorexia	1
		Abdominal cramps	1
Lost weight	13	Voice lost	1
Hemoptysis	9	Night sweats	1
Wheeze	7	Feeling of something in the chest	1
Fatigue	7	Joint pain or arthritis	6

*In one case this was the only symptom.

Roentgenologic Evidence.—All patients had roentgenologic examination of the chest, but the report on one was not available for this study. The findings in the initial roentgenograms of the chest are listed in Table V.

By roentgenogram the lesion was located on the right in fifty-four cases, on the left in thirty-two, and bilaterally in one. The site was not determined in the remainder.

TABLE IV. SIGNIFICANT PHYSICAL SIGNS IN 90 CASES OF SMALL-CELL BRONCHOGENIC CARCINOMA

SIGN	CASES
Dullness over the affected side	56
Breath sounds diminished or absent over the affected side	45
Lag in respiratory movement over the affected side	16
Râles in the chest over the affected side	11
Palpable supraclavicular or axillary nodes	13
Fixed vocal cord (in two of these cases chest negative on physical examination)	6
Bronchial breath sounds over affected side	3
Evidence of superior vena caval obstruction	4
Emaciation	4
Pigmentation on the trunk, face or extremities	2
Palpable liver	2
Audible stridor	2
Deviated trachea	2
Tenderness of chest wall	2
Cyanosis, palpable abdominal mass, nodule in the abdominal wall, clubbed fingers, fixed diaphragm, weakness of one leg	1 each
Physical examination negative	5
Negative except for:	
Stiff shoulders	1
Loss of weight	1
Small "shotty" cervical nodes	1

TABLE V. INITIAL ROENTGENOGRAPHIC FINDINGS IN EIGHTY-NINE CASES OF SMALL-CELL CARCINOMA OF THE LUNG

FINDINGS	CASES
Hilar mass or perihilar infiltration	34
"Atelectasis" of lobes or part of a lung	26
Diffuse opacity, collapse or infiltration of a whole lung	8
Mass at the base of the lung with or without fixation of the hemidiaphragm	5
Infiltration or mass in the midportion of a lung	7
Mediastinal widening only	5
"Bronchiectasis" only	5
Multiple masses in one lung	2
Multiple cavities with mass at the hilus	2
Single cavity	1
Lesion at the costophrenic angle	2
Esophageal displacement by mediastinal mass	1
Condition obscured by opaque oil	1
Negative except for questionable mediastinal widening	1

Bronchoscopic Findings.—Bronchoscopic examination was made in eighty-one cases. In sixty-seven cases a tumor was seen, but biopsy gave positive results in only sixty-two. Examination revealed some deformity of the bronchi in another seven cases. In one case the findings were those of inflammation of the bronchus, and in five cases bronchoscopy gave completely negative results.

Localization of the lesion as determined bronchoscopically is summarized in Fig. 1.

Cytologic Examination of Sputum and Bronchial Secretions.—Adequate study of the sputum or bronchial secretions had been made in thirty-one of the ninety cases of small-cell carcinoma. By adequate study is meant that at least three different specimens were examined before the result could be called negative.

Of the thirty-one cases, carcinoma cells were present and identified in twenty-nine. This represents a diagnostic accuracy of 93.5 per cent. In fourteen of these twenty-nine cases both cytologic and biopsy material were available

for study and of these, in ten the lesion had been diagnosed carcinoma of the small-cell type, and in the remainder it had been diagnosed carcinoma cells, type not specified. Thus, in more than 70 per cent of cases, it was possible to specify cell type as well as diagnose carcinoma.

Treatment.—Since the first successful pneumonectomy for carcinoma by Dr. Evarts Graham was done only in 1933, it is obvious that all the patients in this series could not have had the opportunity of surgical treatment had their lesions been operable at the time. There were, however, only eight cases prior to 1934, so that the majority of the patients could have had surgical treatment if their disease so warranted.

Of the eighty-two patients seen after 1934, only thirty had tumors that were deemed operable, and as one of these refused surgical treatment, there were twenty-nine who were operated on. In other words, about 35 per cent of patients seen were thought clinically to have operable lesions.

Of the twenty-nine patients who underwent thoracotomy, fifteen actually had removal of the lesion, total pneumonectomy being done in every case. In fourteen cases resection was not possible because of extension of the cancer beyond the limits of surgical removal. Details on the duration of life following pneumonectomy in these cases are given in Table VI.

TABLE VI. SMALL-CELL BRONCHOGENIC CARCINOMA: SURVIVAL AFTER PNEUMONECTOMY

SURVIVAL (MONTHS)	PATIENTS	SURVIVAL (MONTHS)	PATIENTS
1	1	12	1
2	1	15	1
3	1	19	1
4	1	26	1
9	4	33	1*
10	1	63	1†

*Operation, January, 1948; alive September, 1950.
†Operation, May, 1945; alive September, 1950.

One patient had bronchoscopic fulguration because of a mistaken diagnosis of adenoma. This patient failed to survive more than six months.

Roentgen Treatment.—Seventeen patients received roentgen treatment. The efficacy of this form of treatment is difficult to evaluate since the effective tumor dose delivered is not known in every case and many patients received palliative or placebo treatment only. None treated with roentgen rays survived longer than a year.

PATHOLOGIC AND CYTOLOGIC ASPECTS OF THE DISEASE

Almost all workers agree on the classification of the cell types, squamous-cell carcinoma and adenocarcinoma, but what to include and exclude in these classifications is not agreed upon. Many group the remainder of the bronchogenic carcinomas as anaplastic or undifferentiated. To illustrate some of the different conceptions regarding classification: Rienhoff[1] considers small-cell (oat-cell) carcinoma, "cylindrical-cell" carcinoma, and adenocarcinoma all as forms of adenocarcinoma, and hence he states that all bronchogenic carcinomas are either adenocarcinomas or squamous-cell carcinomas. Somewhat similarly,

Ormerod[2] lumps all bronchogenic carcinomas as squamous-cell carcinomas or nonsquamous-cell carcinomas. O'Keefe,[3] Björk,[4] and Graham[5] all state that they find it difficult to separate small-cell carcinomas from adenocarcinomas.

In our study no definite evidence could be found to indicate that small-cell carcinoma is an adenocarcinoma subtype. In some cases perithelial grouping of cells gave a pseudoglandular appearance (Fig. 2*a*), but no true acini or alveolar structures were found in any cases.

This study included all those bronchogenic carcinomas with predominantly small cells, regardless of the particular shape they assumed. Thus, in our opinion, the so-called oat-cell cancer, the small round-cell cancer, and the small spindle-cell cancer or "sarcoma" are all simply variations in form of the same tumor.

Gross Characteristics.—Study of the gross surgical specimens revealed that most of the tumors were large, the largest being 15 cm. in diameter. Three patients had small lesions, measuring 1 by 1 by 1 cm., 1.5 by 1.5 by 1 cm., and 1.2 by 0.8 by 1 cm., respectively.

All specimens demonstrated involvement of the hilar nodes by metastatic cancer.

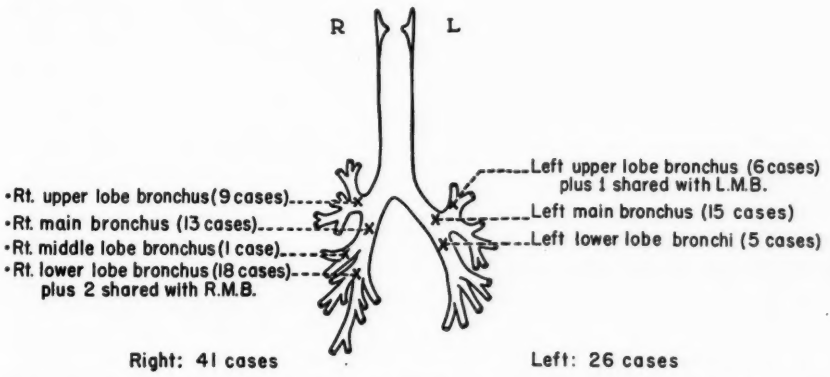
R
L
•Rt. upper lobe bronchus (9 cases)
•Rt. main bronchus (13 cases)
•Rt. middle lobe bronchus (1 case)
•Rt. lower lobe bronchus (18 cases)
plus 2 shared with R.M.B.
Left upper lobe bronchus (6 cases)
plus 1 shared with L.M.B.
Left main bronchus (15 cases)
Left lower lobe bronchi (5 cases)
Right: 41 cases
Left: 26 cases

Fig. 1.—Small-cell bronchogenic carcinoma. Site of the lesions as determined on bronchoscopic examination.

With only one exception the tumors were located either in the main bronchi or in a major secondary bronchus. The one exception was a 15 by 10 by 8.5 cm. tumor in the peripheral portion of the left lower lobe.

All specimens with one exception had evidence of obstructive pneumonitis distal to the bronchial tumor.

Microscopic Aspects.—From the study of tissue in seventy-five of the ninety cases the following characteristics of this group of tumors were noted.

The most constant feature, of course, was the small size of the cells. To determine the size of these cells and nuclei, measurements of cell size using an eyepiece micrometer were made in twenty cases. In each case the nuclei of at least twenty cells taken at random from representative fields were measured. Because poor definition of the cell membrane is one of the characteristics of this

type of tumor a smaller group of actual cell sizes was measured by use of the same method. It was found that the average nuclear diameter was 7.3 microns and the average cell diameter 8.7 microns. Extremes of nuclear size were 3 and 20 microns, but most nuclei fell into the 6- to 8-micron range. For comparison the nucleus of the average lymphocyte measures about 4 microns, and the average polymorphonuclear leucocyte measures about 6 microns (Fig. 2*b*). Thus, compared to many normal cells the malignant cell in question is not small. It is small only in comparison to other malignant cells.

In nearly every case the nuclear-cytoplasmic ratio was high, the nucleus occupying almost 90 per cent of the cell (Fig. 3*a*).

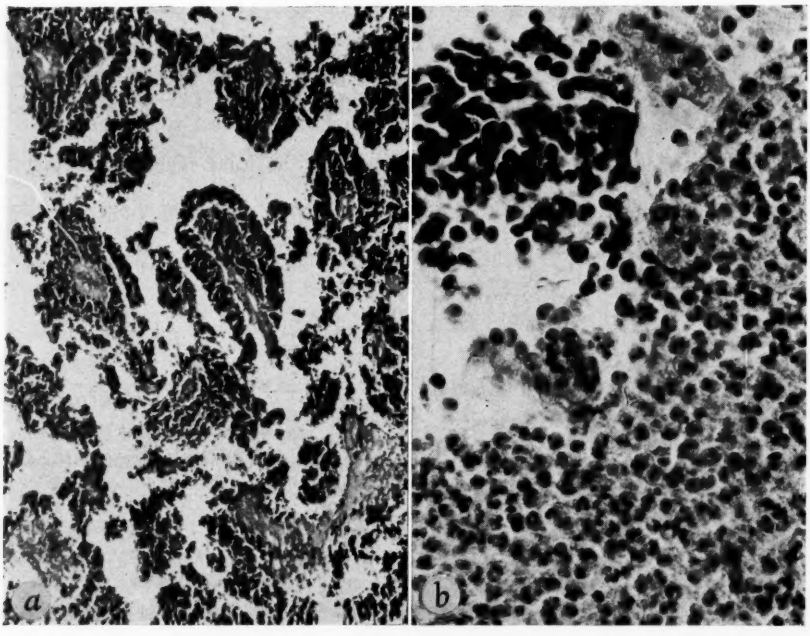

Fig. 2.—Small-cell bronchogenic carcinoma. *a*, Perithelial grouping of cells to give a pseudoglandular appearance (hematoxylin and eosin ×100). *b*, Size of cells of an inflammatory exudate compared with the size of small bronchogenic cancer cells (hematoxylin and eosin ×400).

Hyperchromatism of the nuclei was a prominent feature. In thin sections lightly stained, one could often detect several nucleoli in the nucleus with many fine, scattered, chromatin particles. Most often in the hematoxylin and eosin sections, the nuclei were a solid mass of chromatin. Often one saw only a blob of chromatin material, sometimes spindle-shaped, without any accurate cell or nuclear outlines (Fig. 3*b*). Pleomorphism, giant cells, and very minute cells were present occasionally.

As a rule the cells are closely packed in a medullary form. There is little intercellular stroma nor, as Boyd[6] showed in his cases, do they have intercellular reticulum.

Necrosis forms a very prominent feature of these tumors. This is rarely found in adenomas or lymphosarcomas, and helps in differential diagnosis. Invasion of vessels, lymphatics and adjacent pulmonary tissue and bronchial mucous membrane all were fairly constant features.

Diagnosis of small-cell carcinoma by cytologic examination is based on the finding of numerous cells with a high incidence of more than one of the following[7]: nuclear hyperchromatism, pleomorphism, coarse nucleoli or chromatin granules and a high nuclear-cytoplasmic ratio. Size of cells and nuclei should conform to the average range mentioned. No attempt should be made to diagnose small-cell carcinoma on the basis of a small number of cells, as small histiocytes, lymphocytes, monocytes, and other cells may resemble cancer cells.

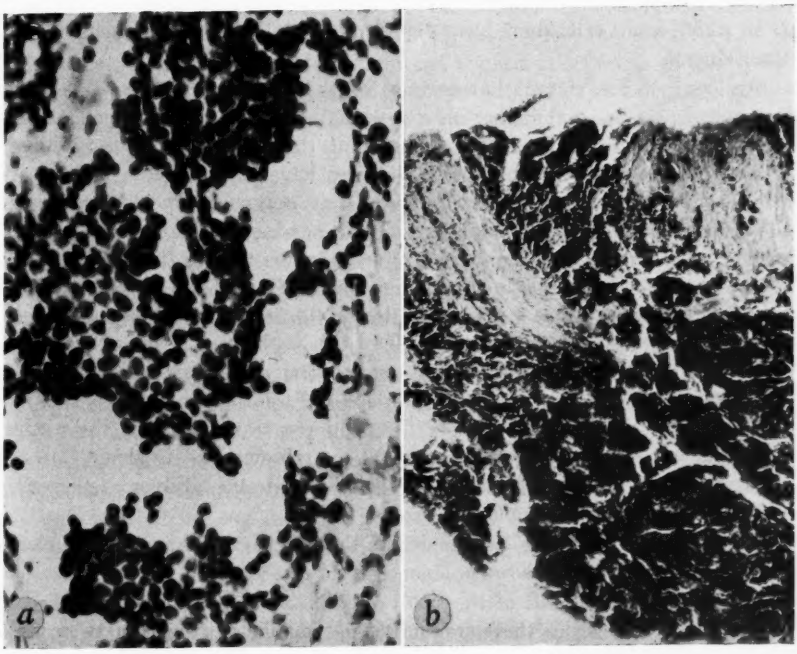

Fig. 3.—Small-cell bronchogenic carcinoma. *a*, High nuclear cytoplasmic ratio with poor outlines of cell membranes (hematoxylin and eosin ×320). *b*, Amorphic mass of chromatin material with poor cell outlines, characteristic of small-cell bronchogenic carcinoma.

COMMENT

Contrary to the belief of Neuhof and Aufses,[8] Tuttle and Womack,[9] Phillips, Basinger, and Adams[10] and also Björk,[4] cell type is a significant prognostic factor and specifically the small-cell carcinoma of the lung is a highly malignant cancer with a poor prognosis, according to the results of our study. Only two survivors, one of whom has had known metastasis, out of ninety cases in forty years' experience, indicates that when this diagnosis is made the outlook is grave indeed.

It is believed that studies of the other cell types of cancer of the lung when correlated with the clinical histories and with this study will indicate that cell type, apart from other clinical factors, will prove to be a most valuable prognostic factor. This view is already held by many,[11, 12] Adams[13] calling it the crux of the whole problem.

The duration of symptoms in most cases makes remote the possibility that small-cell carcinoma is a malignant tumor arising from a previously existing adenoma. There is certainly evidence that adenomas may be, or may go on to become, malignant; however, all the malignant adenomas seen at the clinic were studied as a part of this study, and in every case there was a recognizable difference in the histologic picture from that of the small-cell carcinoma. More study of the malignant adenoma is needed. One should not assume that every case in which small cells show pleomorphism and mitotic figures is one of small-cell carcinoma.

Graham[5, 14] has stated that because of the paucity of necropsy cases of adenoma it is his belief that there is a definite possibility that adenomas become small-cell carcinomas. Abbott[15] has agreed with this belief. Rabin and Neuhof,[16] and also Head[17] have disagreed with this and have stated that a history of a lesion of short duration plus the absence of any polypoid appearance to small-cell carcinomas excludes the possibility of their coming from adenomas. In none of the cases in our series were there any areas in the tumors that resembled the carcinoid or cylindroma pattern of adenomas. If small-cell carcinomas come from pre-existing adenomas, one would expect to find some tissue still present which resembles the parent tumor. At least this is the case in most instances in respect to other malignant tumors that arise from pre-existing benign tumors. The most valuable microscopic criterion for differentiating between small-cell carcinoma and adenoma, aside from the cellular arrangement, is the nuclear-cytoplasmic ratio which is high in small-cell carcinoma and is about 1 to 1 in adenoma. Another feature that aids is the fact that one rarely sees necrosis or spindle-shaped cells in adenomas.

There was no evidence in our study that small-cell cancer could change to another cell type or vice versa.

The evidence that most of the small-cell cancers arise in the larger bronchi seems good; in our series there was only one peripheral tumor in twenty-nine cases in which exploration was done, and in eighty-nine cases in which roentgenograms were available. This is in agreement with the studies of Gebauer,[11] Karsner and Saphir,[18] Koletsky,[19] and others. Few studies have supported the opposite thesis of Tuttle and Womack.[9] This fact of origin in the larger bronchi no doubt helps to explain the high incidence of positive bronchoscopic and cytologic findings in our study.

That these tumors have usually metastasized when one sees them is attested to by the fact that in all cases in our series metastasis either was demonstrable in the surgical specimens or was obvious clinically when the patient was seen. It is felt by many that these tumors metastasize vigorously by lymphatic routes. The evidence of this series seems to favor this view. The data are not complete enough to warrant discussion of metastasis by other routes. Although medias-

tinal nodes were involved in all the surgical specimens, there was no evidence that the primary lesions extended into the mediastinum more frequently than does bronchogenic carcinoma of other cell types.

In regard to treatment this study revealed discouraging but not hopeless results. In spite of what appeared to be occasional beneficial palliative results of roentgen therapy there were no cures with this method of treatment, nor was there evidence of any particular sensitivity to roentgen therapy.

In our series of fifteen patients who underwent pneumonectomy for bronchogenic carcinoma two patients were living at last report. One patient was living more than five years and one was living two years and nine months after operation. The remaining thirteen patients died at intervals ranging up to twenty-seven months after operation. As our knowledge now stands, small-cell carcinoma carries a very poor outlook. Adams[13] had no survivors in his group of surgically treated patients, and one is hard put to it to find any series where more than one or two five-year survivors exist who had proved small-cell carcinoma. In spite of a poor prognosis we cannot agree with Bariéty and others[20] that patients with this type should not be operated on. Surgical treatment continues to offer the only hope for these patients though small it may be.

For this type of carcinoma our study showed a lower operability rate, but approximately the same resectability rate as for carcinoma without distinction as to cell type. In the past few years it has been the tendency both here and elsewhere to do more palliative resections. This will result, of course, in a higher resectability and operability rate, but it is incumbent upon surgeons to indicate that the operation has been a palliative one, when such it is, as it is only with such honesty that true knowledge will result.

Apparently the rate of operability in regard to such malignant tumors would be lower were it not for the fact that these tumors metastasize first to lymph nodes and later to distant sites. Also, it is believed that probably many patients with inoperable growths of this cell type did not have even bronchoscopy and, hence, were not included in our study. This would make the operability rate found in this study falsely high, and the ratio of bronchogenic carcinoma of the small-cell type to bronchogenic carcinoma of all cell types falsely low.

SUMMARY AND CONCLUSIONS

Ninety cases of small-cell carcinoma of the lung were encountered at the Mayo Clinic in the years 1906 through 1948. These constituted 8.8 per cent of all cases of primary bronchogenic carcinoma in which positive tissue proof of the diagnosis was available. The predominant age of occurrence was in the fifth, sixth, and seventh decades. The predominance of males over females was 29 to 1. Race and occupation were not significant factors.

The average duration of symptoms from onset to diagnosis was 5.9 months. Five patients had symptoms for less than one month. Only three patients had symptoms for as long as two years, and for these the evaluation of true symptoms was difficult. The symptoms were identical with those of bronchogenic carcinoma in general; cough, pain in the chest, dyspnea and episodes of pneumonitis were the most frequent. Physical signs also were those

of bronchogenic carcinoma. Dullness over the affected areas, diminished breath sounds, lag in respiration, and râles in the affected areas were the most frequently noted signs.

In all cases in which roentgen examination was made there were positive pulmonary findings with 1 exception in which the interpretation was "negative, possible mediastinal widening." In five cases the interpretation was bronchiectasis, illustrating the danger of accepting the roentgenologic report as the final diagnosis. Further evaluation in all these five cases revealed that the bronchiectasis was secondary to bronchial obstruction by a tumor. There was a slight predominance of lesions in the right side.

Bronchoscopic biopsy gave positive results in 76.5 per cent of cases. In an additional 16 per cent, some evidence of disease was noted but either no lesion was found or biopsy of suspicious areas gave negative results.

Of thirty-one cases in which cytologic examination was done, carcinoma cells were found in twenty-nine, to give a diagnostic accuracy of 93.5 per cent. In more than 70 per cent of the cases in which there was subsequent tissue confirmation it was possible to diagnose the cancer as being of the small-cell type. This indicates that cytologic examination of sputum and bronchial secretions is very helpful when experienced personnel are evaluating the findings.

The pathologic characteristics of small-cell carcinoma are fairly definite and explain in some part the poor prognosis. The only tumors of the lung that offer the pathologist difficulty in differential diagnosis are the atypical adenomas and the true primary lymphosarcoma of the lung. Close study in most cases will reveal the true nature of the tumor.

Of the ninety patients with small-cell bronchogenic carcinoma in this series, twenty-nine underwent exploration, and fifteen of the twenty-nine had pneumonectomy. All the pneumonectomy patients were traced; two were still alive, one five years and four months, and the other two years and nine months, after operation. The last-mentioned patient, however, had a malignant growth removed from the small intestine which probably represented metastasis. All but six of the patients who did not undergo exploration or whose lesion could not be removed surgically were traced; they were all dead. The six untraced patients had definite evidence of hopeless malignancy and must be assumed to be deceased.

Roentgen therapy was given to seventeen patients either at the clinic or in the patient's home community. While several seemed to get good palliative results, there were no survivors in this group.

This study indicates, in our opinion, that small-cell bronchogenic carcinoma is a definite entity and should not be included in the general group of anaplastic or undifferentiated cancer, even though admittedly its behavior is of such a nature. This opinion is based on the fact that there exist (1) a definite, easily recognizable, microscopic picture, (2) a definite high incidence of cytologically positive results on sputum examination which makes the condition easily recognized and diagnosed, and (3) a characteristic clinical behavior.

Finally the results of this study bear out the succinct statement of Dr. Edward Churchill[21]: "The prognosis following surgical extirpation has not

been fully correlated with the predominant cytologic characteristics of cancers of the lung. The evidence that exists, however, confirms the reasonable hypothesis that growths with highly undifferentiated cells are rapidly invasive and tend to metastasize early. The same may be said for the oat cell type. Significant results achieved by the surgical extirpation of cancers of these morphologic types are rare. A biopsy that demonstrates highly undifferentiated or oat cell cancer is presumptive evidence that complete surgical extirpation is a remote possibility."

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BRONCHOGENIC SQUAMOUS-CELL CARCINOMA*

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THE microscopic classification of primary bronchogenic carcinoma now in use at the Mayo Clinic consists of four subdivisions: squamous-cell carcinoma, adenocarcinoma, large-cell carcinoma and small-cell carcinoma. Definite microscopic criteria have been set up for each of these groups. The microscopic criterion required in this study to classify any primary bronchogenic tumor as squamous-cell carcinoma was (1) the presence of intracellular bridges, or (2) definite epithelial pearl formation, or (3) definite keratinization or squamatization, or (4) definite polarization of cells (a whorling tendency) without true pearl formation if accompanied either by minimal squamatization or keratinization or by the typical growth pattern of squamous-cell carcinoma. If any of the first three criteria was found in a single area of any section the tumor was classified as squamous-cell carcinoma. In order to classify a tumor on the basis of only the last criterion, however, more than one area showing the specified characteristics was required.

The characteristic growth pattern of this tumor consists of anastomosing and branching columns of epithelial cells encroaching on the stroma (Fig. 1*a* and *b*.) There is a tendency for the epithelial cells to line up along the edges of these columns, as if in an attempt to form a growing edge of skin. Many squamous-cell carcinomas, however, do not exhibit this growth pattern, and conversely, many large-cell carcinomas do.

Many specimens previously labeled "squamous-cell carcinoma" did not meet the foregoing requirements for this diagnosis. The majority of these were reclassified as large-cell carcinomas, and it was with this group that the major difficulty in classification occurred.

MATERIAL AND METHODS

The records of all cases in the files of the Mayo Clinic through 1949 in which a diagnosis of a tumor of the lung or bronchus had been made and in which positive microscopic proof obtained by bronchoscopy or thoracotomy was available were reviewed. This group involved a study of about 1,400 cases. Of this group, 373 cases met the criteria for primary squamous-cell carcinoma of the bronchus. This study is an analysis of these 373 proved cases.

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Pulmonary resection was performed in 121 cases; in 42 cases of this group resection was performed more than five years prior to the time of this inquiry, and in 89 cases it was done more than two years prior to inquiry. More than 90 per cent of the patients who survived operation were traced.

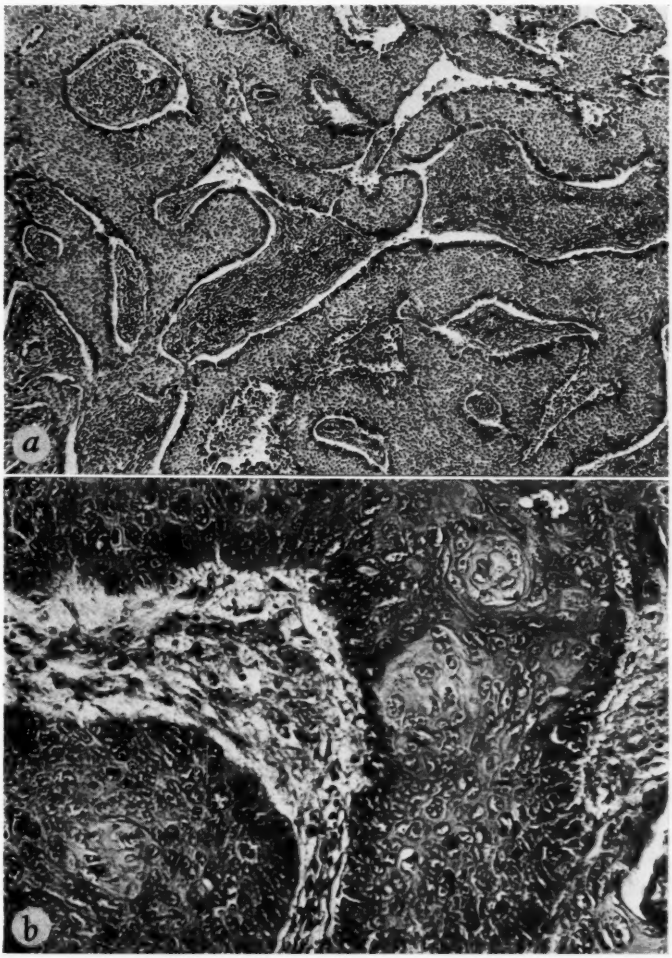

Fig. 1.—Typical growth pattern. Sections stained with hematoxylin and eosin *a*. (×45) *b*. (×200.)

Up through December, 1948, there were 849 proved cases of bronchogenic carcinoma, of which 321 were of the squamous-cell variety, giving an incidence of 37.8 per cent, as compared with 8.8 per cent for small-cell carcinoma, 13.2 per cent for adenocarcinoma, and 40.2 per cent for large-cell carcinoma, for the same period.

PATHOLOGIC CHARACTERISTICS

The 373 squamous-cell carcinomas were graded according to the highest grade of malignancy seen in any section. With this method, 99.5 per cent of the tumors were classified as grade 3 or grade 4 carcinomas. It is not surprising, therefore, that only 13.8 per cent showed true epithelial pearl formation. This hallmark of squamous-cell epithelioma is more characteristically seen in lower grade tumors.

Microscopically the tumor spread mainly in the extracartilaginous portion of the bronchial wall, at times pushing up through the cartilage plates to form an intrabronchial nodule proximal to the main lesion. This is illustrated in Fig. 2, a section separated by 4 mm. of normal mucosa from the main intrabronchial lesion. In situ squamous-cell carcinoma of the bronchial mucosa was also noted in several instances proximal to the gross lesion in the bronchus.

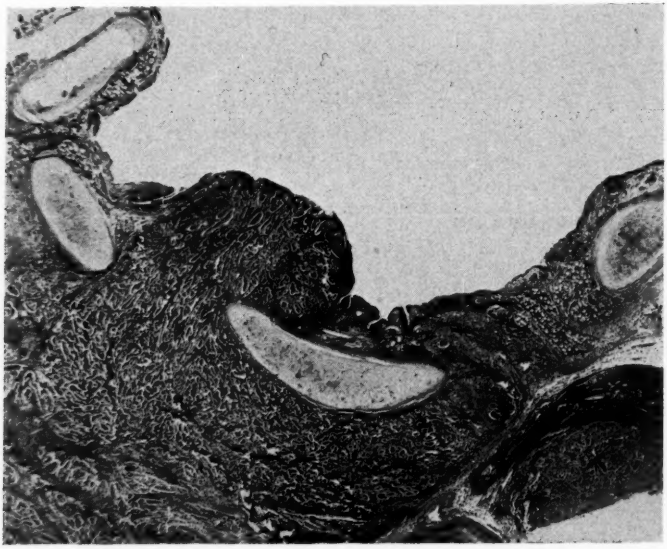

Fig. 2.—View of a "skip" area in an involved bronchus (hematoxylin and eosin ×7.5).

This is not as much a hazard, from the surgeon's viewpoint, as might be anticipated, because in the majority of cases there was obvious gross carcinoma surrounding the bronchus deep to the normal-appearing bronchial mucosa.

Grossly the majority of tumors presented a similar pattern. There was an ulcerated or nodular involvement of a central bronchus with an elliptical mass of carcinoma proximal to and often surrounding the involved bronchus. Lymph nodes were frequently invaded by this mass, but much less frequently were lymph nodes proximal to the gross lesion involved with tumor. Of the 121 cases in which resection was performed, lymph nodes were involved in 43.7 per cent. The average size of the gross tumor was between 2 by 2 by 2 cm. and 5 by 5 by

5 cm., but in some cases the masses were considerably larger, and characteristically more peripherally located, with the involved bronchus seeming to "run into" the mass. It was this type of tumor which sometimes showed a necrotic central abscess. The incidence of abscess formation, however, was only 13 per cent in the group in which resection was performed, and about half of these were in nonmalignant tissue distal to an obstructed bronchus.

The primary growth was located in the right lung in 57.9 per cent of the 121 cases in which resection was performed. The two most frequently involved lobes were the right lower lobe with thirty-five cases and the left upper lobe with thirty cases. In only four cases or 3.3 per cent was the tumor truly periph-

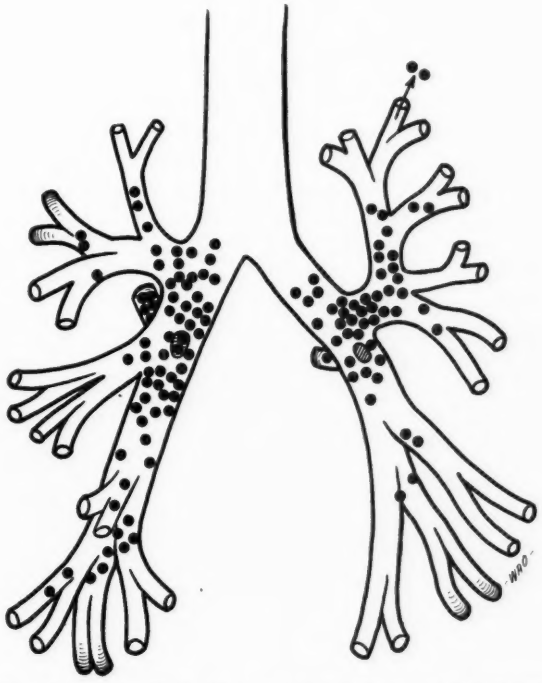

Fig. 3.—Site of the primary growth in 121 cases of squamous-cell bronchogenic carcinoma in in which resection was performed.

eral in location in that it lay more than 4 cm. from the main bronchus or its continuation as the main lower lobe bronchus. Sixty-five and three-tenths per cent of the tumors were in the primary or secondary bronchi, and two-thirds of these were in the main bronchi or the main lower lobe bronchi (Fig. 3).

DIAGNOSIS

Bronchoscopy was performed in more than 99 per cent of the 373 cases, but gave positive results in only 64.5 per cent of the 121 cases in which resection was performed. More than 50 per cent of all tumors located in the right upper

lobe, right middle lobe, or left upper lobe gave negative results on bronchoscopic biopsy, and 44 per cent of those located in the secondary branches of the right lower lobe also gave negative results on bronchoscopic biopsy. In the series in which resection was done, bronchoscopic biopsy gave positive results in 71 per cent of the tumors in the right lung, but in only 53 per cent of those in the left side.

Roentgenologic examination of the chest proved to be the most constant means of determining an abnormal condition in this series. The results of more than 99 per cent of such examinations for the entire group were reported as abnormal. Unfortunately, these findings were rarely diagnostic. The most common findings were obstructive pneumonitis in 42.6 per cent, hilar mass in 28.8 per cent, infiltration of a lobe or part of a lobe in 15.5 per cent, and thickened pleura or bronchiectasis in 10.9 per cent.

In addition to bronchoscopy and the roentgen-ray examination of the chest, a third and more recent addition to the available diagnostic aids in bronchogenic carcinoma is the examination of the sputum or bronchial secretions for malignant cells. Cytologic studies were made in 116 cases in this series including 95 per cent of all the cases encountered from Jan. 1, 1948, through December, 1949. In 72.4 per cent of these 116 cases cytologic studies gave positive results. One hundred patients had cytologic examination of the sputum, with positive results in 63 per cent, and seventy-six patients had cytologic examination of bronchial washings with positive results in 59 per cent.

The clinical findings in this series of cases differed very little from those of most other reported series of bronchogenic carcinoma except that there were fewer patients under 40 years of age in this series. The age range was from 37 to 71 years. The age distribution in this series is shown in Table I.

There were only 13 females (3.5 per cent) in the 373 cases. In the entire group of proved cases of primary bronchogenic carcinoma 10.3 per cent were females.

The duration of symptoms before the definitive diagnosis was established varied greatly but averaged about eight months. The duration in the group with resection was not markedly different from that in the group without resection.

Cough, sputum, hemoptysis, loss of more than 10 pounds, pain in the chest, dyspnea, and fever each occurred in more than 40 per cent of patients in both the group with resection and the group without resection. The presence of pain as a chief complaint and the presence of hoarseness or osteo-arthropathy were each associated with a high incidence of inoperability.

TABLE I. AGE DISTRIBUTION IN 373 PROVED CASES OF PRIMARY SQUAMOUS-CELL BRONCHOGENIC CARCINOMA

AGE, YEARS	CASES	PER CENT OF TOTAL CASES
30-39	6	1.6
40-49	72	19.3
50-59	175	46.9
60-69	117	31.4
70-79	3	0.8
Total	373	100.0

PROGNOSIS WITHOUT PULMONARY RESECTION

The survival rate* for patients without pulmonary resection is shown in Table II for 204 patients who were adequately followed for the indicated period of time. One hundred ninety-two patients were followed two years, and only seven, or 3.6 per cent, survived for two years after the definitive diagnosis was established. There were no three-year survivals.

SURGICAL TREATMENT AND RESULTS

Exploratory thoracotomy was performed on 177 patients. The operation was performed on or after Jan. 1, 1940, in 173 cases, to give an operability rate of 57.7 per cent in the ten-year period from 1940 through 1949. From Jan. 1, 1945, through Dec. 31, 1949, 124 of 175 patients with pathologically proved squamous-cell carcinoma had exploratory thoracotomy. This represents an operability rate of 71 per cent. The significance of these figures is open to some question, however, because cases of bronchogenic carcinoma not verified by biopsy were not included in this series. Perhaps of more importance is the resectability rate in those cases in which exploratory thoracotomy was done. For the ten-year period from 1940 through 1949 pulmonary resection was performed in 120 of 173 thoracotomies, giving a resectability rate of 69.4 per cent. From 1945 through 1949 the resectability rate was 71 per cent.

Pulmonary resection was performed in 121 cases. In forty-two cases the operation was performed more than five years prior to inquiry, and in eighty-nine cases more than two years prior to inquiry. More than ninety per cent of the patients who survived operation were adequately followed. Table III gives the two-year and five-year survival rates for the group with pulmonary resection.

TABLE II. PROGNOSIS FOR 204 PATIENTS WITHOUT PULMONARY RESECTION

PERIOD (MONTHS)	NO OPERATION				EXPLORATORY THORACOTOMY ONLY			
	PATIENTS		LIVED BEYOND INDICATED PERIOD		PATIENTS		LIVED BEYOND INDICATED PERIOD	
	TOTAL	TRACED	NUMBER	PER CENT*	TOTAL	TRACED	NUMBER	PER CENT*
6	195	161	83	51.6	53	43	29	67.4
12	195	159	28	17.6	53	40	11	27.5
18	190	145	13	9.0	49	37	4	10.8
24	187	156	5	3.2	42	36	2	5.6
36	179	151	0	0.0	38	32	0	0.0

*Based on traced patients. Inquiry as of Jan. 1, 1951. Included in the twelve-month group are only those patients operated on twelve months or more prior to the time of inquiry, that is, operated on in 1949 or earlier; included in the eighteen-month group are those patients operated on June 30, 1949, or earlier, and so forth. Hospital mortality is excluded in the calculation of survival rates.

There were seventeen hospital deaths in the 121 cases in which resection was done, giving a hospital mortality rate of 14 per cent. Seventy-nine resections were performed from Jan. 1, 1946, through December, 1949, with only five hospital deaths, giving a hospital mortality rate of 6.3 per cent.

Therefore, given 100 patients with proved primary squamous-cell bronchogenic carcinoma, it can be said on the basis of this study that 71 will be operable, 50 will have resectable lesions, 47 will survive operation, and 24 will be alive in five years.

*The calculations of the survival rates were made by the direct method as described by Berkson and Gage (Proc. Staff Meet., Mayo Clin. 25: 270-286, 1950).

TABLE III. SURVIVAL RATES FOLLOWING PULMONARY RESECTION

PERIOD, YEARS	PATIENTS		LIVED BEYOND INDICATED PERIOD	
	TOTAL	TRACED	NUMBER	PER CENT*
2	75	68	38	55.9
5	30	27	14	51.9

*Based on traced patients. Inquiry as of Jan. 1, 1951. Included in the two-year group are only those patients operated on two or more years prior to the time of inquiry, that is, operated on in 1948 or earlier; included in the five-year group are those patients operated on in 1945 or earlier. Hospital mortality is excluded in the calculation of survival rates.

FACTORS AFFECTING PROGNOSIS

Because of the unexpectedly high survival rate following pulmonary resection, an attempt was made to analyze various factors to determine if they were of prognostic importance. Neither the age of the patient, the duration of symptoms, nor any of the clinical findings was found to affect the prognosis significantly. Similarly, the microscopic grade of the tumor did not affect the prognosis. Since more than 99 per cent of the entire group of tumors had areas of grade 3 or grade 4 carcinoma present, it is doubtful that grading of these tumors is of significance.

Patients with tumors in the right lung had a slightly higher survival rate than those with left-sided lesions. The two-year survival rates for these groups are shown in Table IV.

TABLE IV. THE RELATIONSHIP OF RIGHT-SIDED AND LEFT-SIDED LESIONS TO PROGNOSIS

LOCATION OF LESION	PATIENTS		LIVED 2 OR MORE YEARS AFTER OPERATION	
	TOTAL	TRACED	NUMBER	PER CENT*
Right	44	39	25	64.1
Left	31	29	13	44.8
Total	75	68	38	55.9

*Based on traced patients. Inquiry as of Jan. 1, 1951. Included are patients operated on two or more years prior to the time of inquiry, that is, operated on in 1948 or earlier. Hospital mortality is excluded in the calculation of survival rates.

TABLE V. THE RELATIONSHIP OF INVOLVEMENT OF THE REGIONAL LYMPH NODES TO PROGNOSIS

LYMPH NODE INVOLVEMENT	TWO-YEAR FOLLOW-UP				FIVE-YEAR FOLLOW-UP			
	PATIENTS		LIVED TWO OR MORE YEARS AFTER OPERATION		PATIENTS		LIVED FIVE OR MORE YEARS AFTER OPERATION	
	TOTAL	TRACED	NUMBER	PER CENT*	TOTAL	TRACED	NUMBER	PER CENT*
Positive	28	24	10	41.7	10	8	2	25.0
Negative	47	44	28	63.6	20	19	12	63.2
Total	75	68	38	55.9	30	27	14	51.9

*Based on traced patients. Inquiry as of Jan. 1, 1951. Included in the two-year group are only those patients operated on two or more years prior to the time of inquiry, that is, operated on in 1948 or earlier; included in the five-year group are those patients operated on in 1945 or earlier. Hospital mortality is excluded in the calculation of survival rates.

Regional lymph nodes were involved with carcinoma in 43.7 per cent of the cases in which resection was performed. A sharp fall in the survival rate of those patients with positive findings in the regional lymph nodes was demonstrated only in the five-year follow-up studies, and then in an inadequate num-

ber of cases to be significant. Table V shows the two-year and five-year survival rates for those patients with and without involvement of the regional lymph nodes.

Another factor which seemed to affect the prognosis adversely was the presence of an abscess in the resected specimen. This occurred in 12.4 per cent, and of the eleven patients followed two or more years, only four, or 36.4 per cent, lived two years.

The most significant prognostic finding, however, was the size of the gross lesion. The two-year survival rate for patients with gross lesions smaller than 2 by 2 by 2 cm. was 78.9 per cent, while only 23.1 per cent of patients with lesions larger than 5 by 5 by 5 cm. survived two years (Table VI).

It was then noted that many patients with large gross lesions had a hilar mass reported on their chest roentgenogram, while many patients with small lesions had obstructive pneumonitis but no hilar mass on their chest roentgenogram. Table VII shows the two-year survival rates for patients with various roentgenologic findings in the chest.

TABLE VI. RELATIONSHIP OF THE SIZE OF THE GROSS LESION TO PROGNOSIS

SIZE OF GROSS LESION	PATIENTS		LIVED TWO OR MORE YEARS AFTER OPERATION	
	TOTAL	TRACED	NUMBER	PER CENT*
Smaller than 2 by 2 by 2 cm.	23	19	15	78.9
From 2 by 2 by 2 to 5 by 5 by 5 cm.	39	36	20	55.6
Larger than 5 by 5 by 5 cm.	13	13	3	23.1
Total	75	68	38	55.9

*Based on traced patients. Inquiry as of Jan. 1, 1951. Included are patients operated on two or more years prior to the time of inquiry, that is, operated on in 1948 or earlier. Hospital mortality is excluded in the calculation of survival rates.

These findings strongly suggest that patients with small partially obstructing tumors, shown in the roentgenogram of the chest by obstructive pneumonitis, have a two-year survival rate of approximately 80 per cent. All these patients should therefore have repeated sputum studies and bronchoscopy in an effort to determine if the tumor is of the squamous-cell variety. If so, a very favorable prognosis may be given.

TABLE VII. RELATIONSHIP OF THE ROENTGENOLOGIC FINDINGS IN THE CHEST TO PROGNOSIS

ROENTGENOLOGIC FINDINGS	PATIENTS		LIVED 2 OR MORE YEARS AFTER OPERATION	
	TOTAL	TRACED	NUMBER	PER CENT*
Hilar mass	23	19	9	47.4
Atelectasis without hilar mass	17	16	13	81.3
All others	35	33	16	48.5
Total	75	68	38	55.9

*Based on traced patients. Inquiry as of Jan. 1, 1951. Included are patients operated on two or more years prior to the time of inquiry, that is, operated on in 1948 or earlier. Hospital mortality is excluded in the calculation of survival rates.

SUMMARY

On the basis of definite criteria set up for the diagnosis of primary squamous-cell bronchogenic carcinoma, records of 373 microscopically proved cases were found in the surgical files of the Mayo Clinic through December, 1949. Thirty seven and eight-tenths per cent of all primary bronchogenic carcinomas in this series were squamous-cell in type. Squamous-cell bronchogenic carcinoma rarely occurred under the age of 40. Only 3.5 per cent were females. Bronchoscopy gave positive results in 64.5 per cent of 121 cases in which resection was done. Cytologic examinations gave positive results in 72.4 per cent of 116 cases.

The two-year survival rate in the absence of resection was 3.6 per cent. No patient survived three years without pulmonary resection.

In the five-year period from 1945 through 1949, 71 per cent of 175 patients with pathologically proved lesions had exploratory thoracotomy, and 71 per cent of the 124 thoracotomy patients had pulmonary resection. Both the five-year survival rate and the two-year survival rate for those patients who survived pulmonary resection were more than 50 per cent. Left-sided lesions, lung abscess, and involvement of the regional lymph nodes all affected the prognosis adversely, but the finding of greatest prognostic importance was the gross size of the lesion.

The hospital mortality rate was only 6.3 per cent for seventy-nine pulmonary resections performed from Jan. 1, 1946, through December, 1949.

BRONCHOGENIC ADENOCARCINOMA

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THE differentiation of adenocarcinoma from the other types of bronchogenic carcinoma is based on the microscopic evidence of glandular formation or function. The criterion used is the finding of definite alveolar, acinar, or papillary structures or the formation of extracellular or intracellular mucus, with columnar or cuboidal configuration of the cells (Fig. 1). Of course, all general criteria of malignancy must be met. It should be emphasized that the adenocarcinoma pattern should be predominant or, at the very least, present in a significant number and area of the microscopic sections.

Three specific pitfalls to the correct diagnosis should be mentioned. First, bronchial adenomas should be excluded because of their different origin and behavior. Second, alveolar-cell carcinomas, although probably a definite entity, should be excluded because they arise from the alveolar wall and are therefore not strictly bronchogenic. Third, the bronchial glands in the vicinity of any neoplasm have a tendency to become hyperplastic and disorganized, and, unless care is taken, their appearance may lead one to a false diagnosis of adenocarcinoma.

THE PRESENT STUDY

To the best of our knowledge, all cases in which there was a primary carcinoma elsewhere in the body have been excluded, whether or not we felt that the bronchial lesion was primary. Therefore we believe that the study concerns only the cases of primary adenocarcinoma of the bronchial epithelium. This study is based on 132 cases of adenocarcinoma from the surgical pathology laboratories of the Mayo Clinic through 1949. In forty cases the specimens of tissue were obtained at resection, and in ninety-two cases they were obtained at biopsy, sixty-seven of which represented bronchoscopic biopsy only.

There were 849 proved cases of primary bronchogenic carcinoma through 1948, 112 of which were adenocarcinoma, giving a ratio of 13.2 per cent. This contrasts markedly with other series in the literature in which a higher ratio is shown, but it must be remembered that bronchial adenomas, a large-cell group, and any lesions that might have been metastatic were eliminated.

The youngest patient in this group was 31 years of age, and the oldest 70 years. The average age was 53.3 years. Table I shows the age distribution by decades. It can be seen that more than 90 per cent of the patients were in the age group 40 to 69 years, and nearly half were in the age group 50 to 59 years. There were twenty-six women, representing 19.7 per cent of the total.

In the forty cases in which specimens obtained at resection were available, the point of origin of the tumor was determined as closely as possible. It was decided to regard those lesions in the primary and secondary bronchi as central, and those in the tertiary bronchi or beyond as peripheral (Fig. 2). With this scheme of classifying the tumors, twenty-six of the forty cases in which resection

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TABLE I. AGE DISTRIBUTION IN 132 CASES OF BRONCHOGENIC ADENOCARCINOMA

AGE (YEARS)	CASES	PER CENT
30-39	12	9.1
40-49	28	21.2
50-59	56	42.4
60-69	35	26.5
70	1	0.8
TOTAL	132	100.0
MEAN AGE	53.3 YEARS	

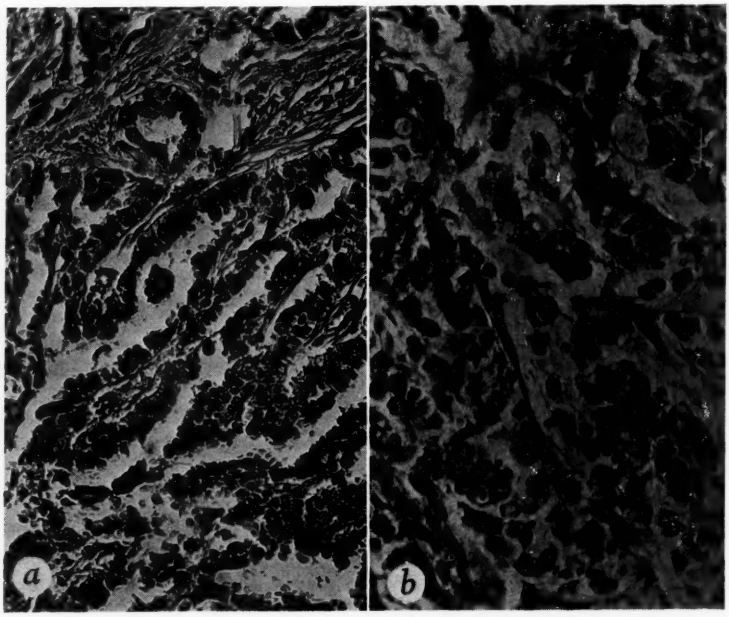

Fig. 1.—*a*, Papillary type of adenocarcinoma (hematoxylin and eosin ×150). *b*, Mucus-producing type of adenocarcinoma with both extracellular mucus and signet-ring cells (hematoxylin and eosin ×160).

was performed (65 per cent) were found to represent peripheral lesions, and fourteen cases (35 per cent) represented central lesions (Fig. 3).

Thirty-six of the patients underwent bronchoscopy prior to operation; in nine of these bronchoscopic biopsy gave positive results. All those with positive results on biopsy had lesions that were judged as being centrally located when the gross surgical specimen was examined. While these nine patients with positive results on biopsy represented only 25 per cent of the total patients who underwent bronchoscopy, they nevertheless represented 64.3 per cent of the cases in which the lesions were centrally situated.

The symptoms were in generally those of any type of bronchogenic carcinoma. The five most prominent symptoms were cough, pain, loss of weight, hemoptysis, and dyspnea in the following incidence: cough, 83.8 per cent; pain or aching in the chest, 49.6 per cent; loss of weight, 48.7 per cent; blood-streaked sputum or hemorrhage, 47.0 per cent; and dyspnea, 24.1 per cent. The average

duration of symptoms from onset to histologic diagnosis was 7.9 months for the cases in which biopsy only was performed, either bronchoscopically or surgically, and 6.8 months for the cases in which resection was done. Details are given in Table II.

Cytologic examination of the sputum and bronchial secretions for malignant cells was done in fifty-one cases, and such cells were found in thirty-two cases (62.7 per cent). Of the nineteen cases in which negative results were obtained, in twelve the examinations were judged inadequate, that is, less than three specimens for cytologic examination were received in the laboratory. With these cases excluded, cytologic examination gave positive results in 82.1 per cent of the adequate examinations.

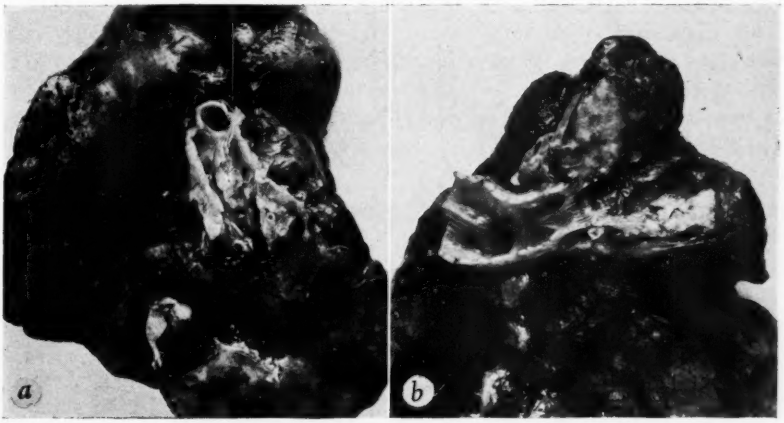

Fig. 2.—*a*, Typical central bronchogenic adenocarcinoma in the bronchi of the main and lower lobes of the right lung. *b*, Typical peripheral bronchogenic adenocarcinoma in the apex of the left lung.

From 1940 through 1944 there were forty-four cases; in thirteen of these (29.5 per cent) exploration was carried out, and in five cases (11.4 per cent) resection was done. Thus resection was done in 38.5 per cent of the cases in which exploration was carried out. From 1945 through 1949 there were sixty-seven cases, with forty-six explorations and thirty-four resections. This gives an exploration rate of 68.7 per cent, and a resection rate of 50.7 per cent. In 73.9 per cent of the cases in which exploration was done, resection was carried out. Apparently the higher resection rate of the latter group is due partially to a higher rate of exploration and partially to an increase in the cases selected for resection at exploration.

In three of the cases, reports of roentgenologic examination were not available. In all the remainder, abnormalities were found in the roentgenograms of the chest, but it was felt that in 12 per cent of these cases bronchogenic carcinoma was not suspected. In the cases in which it was judged that carcinoma was unsuspected on roentgenologic examination, such diagnoses as "tuberculosis," "empyema with tuberculosis," and "bronchiectasis" were the most common. In the remainder of the cases, or 88 per cent, it was felt that bronchogenic carcinoma was either suspected or should have been. Such diagnoses as "mass

in the right midlung field," "bronchial obstruction with atelectasis," or "atelectasis" alone, as well as "bronchogenic carcinoma" or "rule out malignancy" were accepted as evidence that primary bronchogenic carcinoma was suspected.

On attempting to grade the lesions according to the method of Broders, we were immediately faced with the problem that the individual cases not only varied as to cell type throughout the lesion, but that they varied likewise as to

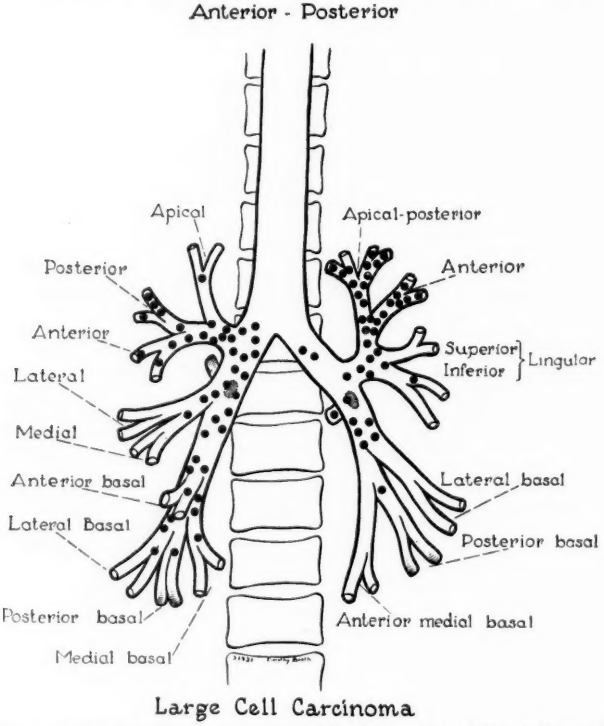

Fig. 3.—Position of the tumor in forty cases of bronchogenic adenocarcinoma in which resection was performed (anteroposterior view). Each dot represents an individual case.

grade. It was felt, however, that the grade should be called according to the highest grade found in the lesion, since presumably that portion of the tumor would be the most malignant and the most likely to metastasize. It was found that there was rarely more than one grade difference in an individual tumor;

TABLE II. DURATION OF SYMPTOMS IN 132 CASES OF BRONCHOGENIC ADENOCARCINOMA

DURATION OF SYMPTOMS, MONTHS	SOURCE OF SPECIMEN	
	BIOPSY, PER CENT OF 92 CASES	RESECTION, PER CENT OF 40 CASES
ASYMPTOMATIC	2.2	20.0
1-3	17.4	22.5
4-6	26.1	22.5
7-9	21.7	10.0
10-12	20.7	5.0
13-24	12.0	17.5
25-36	0	2.5
MEAN	7.9 MONTHS	6.8 MONTHS

that is, if we found a tumor which we graded 3, there might be and usually was a significant portion of the tumor which could be graded 2, but rarely any portion of the tumor which could be graded 1. Using this system we found that 117 of the 132 lesions, or 88.6 per cent, were grade 3 and grade 4, while fourteen lesions, or 10.6 per cent of the total, were grade 2, and one lesion was grade 1. Thus most of the patients had high grade lesions.

Pneumonectomy or lobectomy for carcinoma of the bronchus was performed on forty patients of this series, with six hospital deaths (15 per cent). These operations are rather recent procedures in surgery, and this fact was evident when we tried to get an idea about prognosis in this group. Only sixteen patients in the series were operated on prior to 1947, and nearly half of the patients were operated on in 1948 or 1949. For this reason we felt that prognosis* could be logically calculated only on a short-term basis (Table III). More than one-half of the patients who were operated on are alive at the end of one year, and a third will be alive two years after operation. This indicates that the prognosis in this type of bronchogenic carcinoma is poor, but it will take the test of time to prove whether or not the prognosis is as bad as is indicated by this series. A

TABLE III. SURVIVAL RATES FOR PATIENTS WITH BRONCHOGENIC ADENOCARCINOMA FOLLOWING PNEUMONECTOMY OR LOBECTOMY

PERIOD, YEARS	PATIENTS		LIVED BEYOND INDICATED PERIOD	
	TOTAL	TRACED	NUMBER	PER CENT*
1	34	28	16	57.1
2	23	21	7	33.3

*Based on traced patients, inquiry as of Jan. 1, 1951. Included in the one-year group are only those patients operated on one or more years prior to the time of inquiry, that is, operated on in 1949 or earlier; the two-year group includes only those patients operated on in 1948 or earlier. Hospital mortality is excluded in the calculation of survived rates.

breakdown of the seven patients who survived two or more years following operation revealed that three patients died during the third year following operation, and the remainder were still alive: one was alive during the third year following operation, two were alive during the fifth year, and one was alive more than ten years following operation. This at least indicates that though the prognosis may be bad it is not hopeless, and some patients may survive for relatively long periods after operation.

SUMMARY

The criteria for diagnosis of bronchogenic adenocarcinoma have been presented, and certain aspects of diagnosis reviewed. It was found that 13.2 per cent of all primary carcinomas in this series were adenocarcinomas, and that about one-fifth of the patients were females. The majority of tumors were of peripheral origin which was reflected in the low rate of positive results on biopsy. Cytologic examination gave positive results in about 80 per cent of cases. Apparently symptoms, age distribution, and roentgenologic findings were similar to those of other types of bronchogenic carcinoma. The prognosis is apparently poor, since two years after operation two-thirds of the patients who survive resection die.

*The calculations of the survival rates were made by the direct method as described by Berkson and Gage (Proc. Staff Meet., Mayo Clin. 25: 270-286, 1950).

BRONCHOGENIC LARGE-CELL CARCINOMA

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THE microscopic diagnosis of the large-cell type of bronchogenic carcinoma is primarily a diagnosis of exclusion. In examination of the tissue in any large group of cases of bronchogenic carcinoma, it is possible to separate a group of typical squamous-cell carcinomas and a group of small-cell carcinomas according to the microscopic criteria given elsewhere in this series of papers. We chose to adhere strictly to the criteria given for small-cell carcinomas, and to put in the squamous-cell group every case in which there was definite evidence of squamous-cell criteria as given elsewhere. Separation of these two groups leaves one with a group of adenocarcinomas and a group in which a specific type of carcinoma cannot be diagnosed with any certainty. For the latter cases a diagnosis of high-grade carcinoma, type indeterminate, would seem to be the most valid one. It is these cases that we have chosen to call "large-cell carcinomas," both because by this means it is possible to bring them together for easy reference, and because in most of the cases the lesions are characterized by being composed of relatively large cells. Unfortunately, however, the border of differentiation between adenocarcinoma and large-cell carcinoma cannot be so easily defined as that between large-cell carcinoma and squamous-cell carcinoma, or between large-cell carcinoma and small-cell carcinoma. We have chosen, therefore, to be as strict as possible in defining adenocarcinomas by saying that the adenocarcinoma pattern must be present in a majority of the microscopic sections and in a significantly large area as stated in another paper of the series.

The cellular pattern of the large-cell group is bizarre with marked variation in the staining qualities and size of the individual cells. The nuclei tend to be large and rather dark with prominent nucleoli, there may be many mitotic figures, and there may be giant-cell forms. The cells may be angular, oval, or spindle-shaped, and they tend to be closely packed in a medullary or pseudoalveolar arrangement. Nearly always there are areas of necrosis which may show fragmented bits of cells intermingled with leucocytes, which may be hemorrhagic, which may be fibrotic, or which may show any combination of these. There also is usually evidence of a highly malignant potential, both as to local destruction of tissue and as to invasion of lymphatics and blood vessels (Fig. 1).

THE PRESENT STUDY

In this study all cases in which there was a primary carcinoma elsewhere in the body were eliminated to the best of our knowledge, whether or not we

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felt that the bronchial lesion was primary. The study is based on 384 cases of large-cell carcinoma encountered in the surgical pathology laboratories of the Mayo Clinic through 1949. These were made up of 87 cases in which the specimens were obtained at resection and 297 cases in which they were obtained for biopsy, 255 representing bronchoscopic biopsy only.

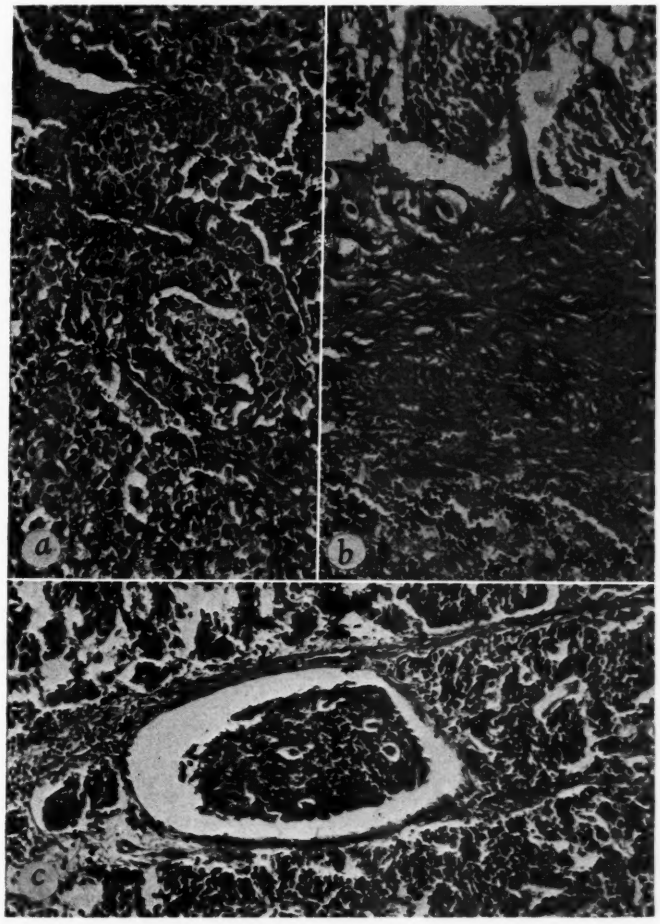

Fig. 1.—*a*, A typical large-cell carcinoma with punched-out areas of necrosis, making the section resemble an adenocarcinoma (hematoxylin and eosin ×110). *b*, A large-cell carcinoma showing necrosis and fibrosis. This was taken from a large area of necrosis, and shows the border of the malignant cells (hematoxylin and eosin ×110). *c*, A large-cell carcinoma showing a plug of carcinoma cells in a lymphatic channel (hematoxylin and eosin ×110).

Through 1948, 849 proved cases of bronchogenic carcinoma had been found at the clinic, of which 341, or 40.2 per cent, were of the large-cell type. Large-cell carcinoma made up the largest group, squamous-cell carcinoma constituting 37.8 per cent, adenocarcinoma 13.2 per cent, and small-cell carcinoma 8.8 per cent of the total.

In the series of 384 cases the youngest patient was 22 years old, the oldest 80 years of age. The average age was 55 years. The age distribution by decades is given in Table I. It can be seen that more than 90 per cent of the patients were in the age group 40 to 69 years, and nearly half were in the group 50 to 59 years. This is about the same ratio as that for the other types of bronchogenic carcinoma, nearly all the patients being over 40 years of age.

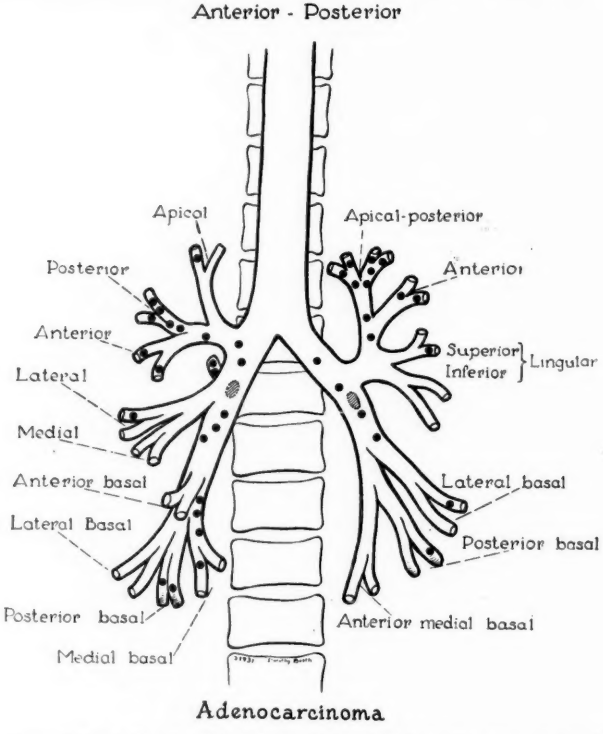

Fig. 2.—Location of the lesion in eighty-five of the eighty-seven cases of resection in which location could be determined (anteroposterior view).

There were fifty-six females in the group, representing 14.6 per cent of the total. This is close to the percentage of 19.7 for females with adenocarcinoma, and it contrasts markedly with the percentage of 3.5 for females with squamous-cell carcinoma and 3.3 for females with small-cell carcinoma.

The eighty-seven surgical specimens were examined grossly. Lesions in the primary or secondary bronchi were classified as central, and those in the tertiary bronchi or beyond as peripheral. It was found that fifty lesions, or 57.5 per cent, were central and that thirty-seven, or 42.5 per cent, were peripheral, giving a ratio of 1.4 to 1. The ratio of central to peripheral lesions for each of the other three types of bronchogenic carcinoma was as follows: small-cell carcinoma 27.7 to 1; squamous-cell carcinoma, 1.9 to 1; and adenocarcinoma,

0.54 to 1. In most of the cases the lesion was in the right main, upper, and lower lobe bronchi and in the left upper lobe (Fig. 2). The left lower lobe was apparently rarely involved. This same phenomenon was observed in the adenocarcinoma group and in the squamous-cell carcinoma group, but whether this was real or only apparent and whether we were missing those lesions in the left lower lobe is impossible at this time to determine.

TABLE I. AGE DISTRIBUTION BY DECADES IN 384 CASES OF BRONCHOGENIC LARGE-CELL CARCINOMA

AGES, YEARS	CASES	PER CENT
20-29	3	0.8
30-39	18	4.7
40-49	59	15.4
50-59	179	46.6
60-69	117	30.4
70 OR MORE	8	2.1
TOTAL	384	100.0
MEAN AGE	55.0 YEARS	

In seventy-five of the cases in which resection was performed, bronchoscopy was carried out prior to operation and positive results on biopsy were obtained in thirty-one of these. In all those in which biopsy gave positive results the lesion was shown to be central at the time of resection. These thirty-one cases represented only 41.3 per cent of the cases in which bronchoscopy was performed, but they represented 62 per cent of all the central lesions.

Symptoms present were, in general, those of any type of bronchogenic carcinoma. The five commonest symptoms were cough, loss of weight, pain, hemoptysis, and dyspnea in the following incidence: cough, 80.7 per cent; loss of weight, 54.4 per cent; pain or aching in the chest, 47.9 per cent; blood-streaked sputum or hemorrhage, 44.0 per cent; and dyspnea, 29.5 per cent. The average duration of symptoms from onset to histologic diagnosis was 8.4 months in the cases in which biopsy was done and 6.4 months in the cases in which resection was performed (Table II).

Cytologic examination of the sputum and bronchial secretions for malignant cells was performed in 144 cases and malignant cells were found in 111, or 77.1 per cent. Cytologic examination was judged as inadequate in twenty of the thirty-three cases in which the results were negative, that is, inadequate in that less than three specimens for examination were received in the laboratory. With these excluded, cytologic examination gave positive results in 89.5 per cent of the cases in which an adequate number of specimens were available.

From 1940 through 1944 there were 105 cases, in thirty-four of which exploration was carried out; resection was done in twelve of the thirty-four cases. This gives an exploration rate of 32.4 per cent, a resection rate of 11.4 per cent, and a ratio of resection to exploration of 35.2 per cent. From 1945 through 1949 there were 200 cases, in 116 of which exploration was performed; in 65 of the 116 resection was done. This gives an exploration rate of 58 per cent, a resection rate of 32.5 per cent, and a ratio of resection to exploration of 56

TABLE II. DURATION OF SYMPTOMS IN 384 CASES OF BRONCHOGENIC LARGE-CELL CARCINOMA

DURATION OF SYMPTOMS (MONTHS)	SOURCE OF SPECIMEN	
	BIOPSY (PER CENT OF 297 CASES)	RESECTION (PER CENT OF 87 CASES)
ASYMPTOMATIC	2.4	12.6
1-3	22.9	24.1
4-6	30.0	29.9
7-9	15.2	14.9
10-12	13.8	4.6
13-24	12.8	10.3
25-36	2.7	3.4
MEAN	8.4 MONTHS	6.4 MONTHS

per cent. Apparently the higher resection rate in the latter group was due both to a higher rate of exploration and to a higher rate of resection in the cases in which exploration was done.

In ten cases, reports of roentgenologic examination were not available. Of the remainder, in eight the roentgenograms were reported as normal, and in five they were reported as normal, but the notation was made in the latter cases that the pulmonary fields were obscured by residual oil. In all the remaining cases there were abnormal roentgenologic findings, but it was felt that in 12.5 per cent of these, bronchogenic carcinoma was not suspected. In those in which we felt that bronchogenic carcinoma was not suspected, the diagnosis most often made was pulmonary tuberculosis.

With this cell type of bronchogenic carcinoma there is no grading problem, because by definition all the lesions must be grade 4.

It has already been pointed out in this series of papers that resection of portions of the lung for carcinoma has been rather a recent development in surgery. There were twelve hospital deaths (13.8 per cent) among the eighty-seven patients in this group. Only twenty-six of eighty-seven patients were operated on before 1947, and forty-one, or nearly half, were operated on during 1948 or 1949. It was felt, therefore, that survival rates* should be calculated only on a short-term basis (Table III). Forty-eight and six-tenths per cent of the patients were dead in a year, and 56.4 per cent were dead within two years. A breakdown of the twenty-four patients who lived two or more years following operation is as follows: six patients died in the third year following operation, one in the fourth year, and three in the fifth year; five patients are living in the third year following operation, five in the fourth year, two in the fifth year, and two patients are still living more than ten years following operation. This indicates that prognosis is poor in this type of bronchogenic carcinoma, but perhaps not as bad as that for bronchogenic adenocarcinoma or small-cell carcinoma and not nearly as good as that for squamous-cell carcinoma. The reader will recall that the large-cell type of bronchogenic carcinoma is the one in which the cells are so anaplastic that no more specific type of microscopic diagnosis should be made than that of "high-grade carcinoma, type indeterminate." These, therefore, should logically be the most malignant and carry the poorest

*The calculations of the survival rates were made by the direct method as described by Berkson and Gage (Proc. Staff Meet., Mayo Clin. 25: 270-286, 1950).

prognosis of all types of bronchogenic carcinoma with the exception of the small-cell type. We have taken the surprising survival of some of these patients to mean that a goodly proportion of the lesions actually must be squamous-cell carcinomas which are of such high grade that they cannot be so diagnosed, and yet carry over some of the better prognosis to be expected of the squamous-cell type of bronchogenic carcinoma.

TABLE III. SURVIVAL RATES FOR PATIENTS WITH BRONCHOGENIC LARGE-CELL CARCINOMA FOLLOWING PNEUMONECTOMY OR LOBECTOMY

PERIOD, YEARS	PATIENTS		LIVED BEYOND INDICATED PERIOD	
	TOTAL	TRACED	NUMBER	PER CENT*
1	75	74	38	51.4
2	56	55	24	43.6

*Based on traced patients, inquiry as of Jan. 1, 1951. Included in the one-year group are only those patients operated on one or more years prior to the time of inquiry, that is, operated on in 1949 or earlier; the two-year group includes only those patients operated on in 1948 or earlier. Hospital mortality is excluded in the calculation of survival rates.

SUMMARY

The criteria for diagnosis of bronchogenic large-cell carcinoma have been presented, and the microscopic relation to other types of bronchogenic carcinoma reviewed. It was found that 40.2 per cent of the bronchogenic carcinomas in this series were of the large-cell type, and that 14.6 per cent of the patients were females. Age distribution, symptoms, and roentgenologic findings were similar to those in other types of bronchogenic carcinoma. The ratio of central to peripheral lesions was found to be 1.4 to 1 for large-cell carcinoma, as compared with 1.9 to 1 for squamous-cell carcinoma, 27.7 to 1 for small-cell carcinoma, but with 0.54 to 1 for adenocarcinoma. Cytologic diagnosis gave positive results in nearly 90 per cent of adequate examinations. About 55 per cent of the patients who survive resection die within two years. This indicates a poor prognosis in this type of bronchogenic carcinoma, but perhaps the prognosis is not as bad as that for bronchogenic adenocarcinoma or small-cell carcinoma, and not nearly as good as that for squamous-cell carcinoma.

HEMODYNAMICS: STUDIES ON A GROUP OF PATIENTS WHO DEVELOPED COR PULMONALE FOLLOWING THORACOPLASTY

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KYPHOSCOLIOSIS has been recognized as a cause of heart disease for many years. Thoracoplasty has been mentioned as a cause for cor pulmonale, but has received little attention in medical literature. It is the purpose of this paper to report on physiologic observations in a group of five patients who developed cor pulmonale within eight to fifteen years following thoracoplasty. No special effort or case finding was made to detect these cases. They were gleaned from a series of over 650 cardiac catheterizations carried out under the direction of the author.

METHOD

The patients were studied in the basal state with administration of 0.06 Gm. Nembutal one hour before catheterization. The cardiac outputs, done in duplicate, were determined by the direct Fick principle. The oxygen consumption of the patient was determined by measuring the volume of inspired air on a specially designed gas meter,[1] and the oxygen content of the expired air and of the room air was determined by means of a Pauling oxygen analyzer. The blood oxygen contents were determined by the spectrophotometric method of Hickam and Fraser.[2] Pressures in the femoral artery and from the right side of the heart, as well as the electrocardiograph and phase of respiration, were recorded on a six-channel oscillograph by means of Statham gauges and strain amplifiers.[3]

CASE REPORTS

A clinical résumé of the five cases studied is as follows:

CASE 1.—B. G., aged 24 years, female. Ten-rib left thoracoplasty fourteen years ago for tuberculosis. The patient did well until one month ago when she contracted a cold. Physical examination: vital capacity, 40 per cent of normal; P_2 greater than A_2; P_2 shock was felt. Right ventricle was active. Regular sinus rhythm. Right axis deviation in the electrocardiogram and pulmonale P waves. On fluoroscopy there was a large pulmonary artery.

CASE 2.—C. B., aged 39 years, male. Eight-rib thoracoplasty on left in 1937, for tuberculosis. Upper six ribs and corresponding second stage in November, 1937. Third stage consisted of transverse processes in 1938. History of cardiac failure for three weeks prior to admission. Summary of cardiac findings showed P_2 to be greater than A_2. There were no murmurs, regular sinus rhythm. The electrocardiogram showed the heart was verticle with tendency to right axis deviation, and peaked P waves, Leads II and III. Fluoroscopy of the heart was unsatisfactory due to distortion caused by preceding operations. Vital capacity was 34 per cent of normal.

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CASE 3.—M. V., aged 33 years, female. First stage, left thoracoplasty in October, 1941, with vital capacity 36 per cent of normal. Second stage, posterolateral in November, 1941—anterolateral cartilages 1, 2, and 3, and anterior segments of 2, 3, and 4, and peaked P waves in Leads II and III. Vital capacity was 30 per cent of normal. Third stage, eight-rib anterolateral in January, 1942, with vital capacity 30 per cent of normal. Cardiac findings: loud P_2, regular sinus rhythm. The electrocardiogram showed large P waves, right axis deviation. Prominent pulmonary artery on fluoroscopy.

CASE 4.—M. C., aged 41 years, male. Seven-rib thoracoplasty in December, 1939. Vital capacity was 55 per cent of normal. Cardiac findings: P_2 greater than A_2, regular sinus rhythm, no murmurs. The electrocardiogram showed prominent P waves, Leads II and III. Fluoroscopy unable to evaluate due to distortion of chest wall. Vital capacity in May, 1940, was 51 per cent of normal. At time of study vital capacity was 44 per cent.

CASE 5.—A. R., aged 50 years, male. Tuberculosis with emphysema since 1933. Oleothorax followed by thoracoplasty and phrenic crush in 1936. First stage on March 4, 1936, vital capacity was 52 per cent of normal. Second stage on March 28, 1936; vital capacity was 28 per cent. Third stage on April 18, 1936; vital capacity was 30 per cent. The three operations resulted in the removal of varying lengths of ribs one to ten and the corresponding transverse processes. Four months before study he began to develop shortness of breath. Cardiac findings: A_2 greater than P_2, regular sinus rhythm, no murmurs. It was difficult to interpret heart size due to chest deformity. The electrocardiogram showed left axis deviation. Semi-horizontal heart, moderate right and left ventricular hypertrophy. On fluoroscopic examination the pulmonary arteries were prominent, and the right ventricle appeared slightly enlarged.

RESULTS

Table I summarizes the results of the physiological studies in these five cases. All had marked elevation in pulmonary artery pressure, and pulmonary resistance was markedly increased. The pulmonary diastolic pressures were markedly elevated from 100 to 500 per cent above normal. The above changes are consistent with those found in another group of patients studied who had cor pulmonale from a variety of causes.[4]

Pulmonary capillary pressures were measured in two patients, and were found within the range of normal. Dexter[5] was the first to show that patients with cor pulmonale had normal pulmonary capillary pressures. This has been confirmed by us.

The problem of cardiac output in patients with cor pulmonale still is not clear. We have observed patients with cor pulmonale in failure without elevated cardiac outputs, and again we have observed elevated outputs in patients with cor pulmonale and congestive failure.[4] It would appear that the degree of anoxia and the amount of low-grade chronic infection that is present in the lungs of this type of patient determine, in a sense, the output gradient.

DISCUSSION

It is of interest why patients with thoracoplasty should develop cor pulmonale, if the remaining lung has no disease. In these five patients the disease was limited to one lung.

Ackerman and Kasuga,[6] in 1941, conducted a survey of the various changes in pulmonary tuberculosis which tended to affect the right side of the heart with hypertrophy of the ventricular wall as a result. In this connection they stressed that chronic productive tuberculosis with emphysema, marked pneumothorax

TABLE I. SUMMARY OF HEMODYNAMICS IN A GROUP OF FIVE PATIENTS WHO DEVELOPED COR PULMONALE FOLLOWING THORACOPLASTY*

NAME	PULMONARY ARTERY PRESSURE		FEMORAL ARTERY PRESSURE		RIGHT VENTRICLE	RIGHT AURICLE	PULMONARY CAPILLARY PRESSURE	CARDIAC INDEX	CARDIAC OUTPUT	SYSTEM RESISTANCE (DYNES/CM.^{5})	PULMONARY RESISTANCE (DYNES/CM.^{5})	HEART RATE	STROKE VOLUME (C.C.)
	MM.HG.	MEAN	MM.HG.	MEAN									
V., M. 33 W., F.	90/52	68	96/67	75	96/10	14/3		3.34 L.	4.65 L.	1795	1621	100	46
B., C. 39 W., M.	34/20	24	210/125	145	30/2	5/3	3.5 M.P.	3.82 L.	6.29 L.	3150	510	107	59
G., B. 24 W., F.	57/29	38	93/63	80	53/0	4.3/–2		4.34 L.	5.02 L.	1480	705	100	50
R., A. 50 B., M.	41/20	28	116/63	87	37/0	4.4/1	5 M.P.	2.60 L.	4.45 L.	2680	857	73	61
M., C. 41 B., M.	38/23	29	119/84	103	40/2	6/3.5		5.16 L.	10.92 L.	1590	445	91	120

*Note: Pulmonary capillary pressure was measured in two of the patients in this group and was found in the range of normal.

of long duration, and thickened pleura, sometimes gave rise to the right side hypertrophy. Finally they claimed thoracoplasty may be a factor in the production of the right-sided ventricular hypertrophy.

Higgins,[7] in 1944, in a series of 600 autopsy cases of pulmonary tuberculosis, observed a slight increase in the weight of the right ventricle. He was unable to find a correlation between right-side hypertrophy and individual collapse therapy, although he did observe a correlation with the duration of the disease.

Griggs, Coggin, and Evans[8] studied a series of 18,000 autopsied cases with a view to ascertaining the extent to which chronic pulmonary diseases led to cor pulmonale. They found the wall of the right ventricle at least 0.5 cm. thick in more than 50 per cent of the cases of emphysema, but in only 3.7 per cent of the 1,470 cases of pulmonary tuberculosis.

However, the great numerical superiority of the latter cases meant that they found hypertrophy of the right ventricle more often in cases of pulmonary tuberculosis than in any other disease of the lungs.

Gibbon, Hopkinson, and Churchill,[9] in 1932, showed in animal experiments that signs of cor pulmonale did not appear until at least 60 per cent of the blood flow through the pulmonary artery had been cut off. Recently, we have shown that although there is a transitory marked rise at the time of tying off of the right or left pulmonary artery during a pneumonectomy, this pressure soon begins to return to a normal level by compensation of the remaining vascular bed, and usually by the time this operation is completed, the pressure had returned to preoperative levels.[10]

Cournand[11] has also shown in studies that the pressures in the pulmonary artery, after patients have had pneumonectomy, are still in the normal range if they had no disease in the remaining lung. He has measured pressures in the pulmonary artery several years after pneumonectomies and has found normal values.

Bruce[12] reported on two cases of thoracoplasty who developed cor pulmonale, proved at autopsy. He emphasized the fact that after operation the thoracoplastic patient often showed a striking gross anatomic resemblance to the kyphoscoliotic patient, as usually a deformity of the chest develops in connection with the operation, and this deformity involves the spine and gives rise to a more or less pronounced spinal curvature, with the convexity to the operated side. Bruce also pointed out that in spontaneous thoracic deformities, scoliosis, with the convexity on the right side, is for some reason more common than scoliosis with left side convexity. It has been claimed that cardiac pulmonary insufficiency, especially, tends to appear when the deformity is accompanied by right-sided compensatory compressions of the left side of the thorax which, in turn, has a specific effect on the heart and the conditions under which it functions. Three of our five cases had left-sided thoracoplasties.

Certain it is that thoracoplasty has a great deal to offer the selected case of tuberculosis. However, one of the complications that a patient with a thoracoplastry may encounter is cor pulmonale. It would also seem difficult to predict

the patient who will develop cor pulmonale following thoracoplasty. Certainly it is, the more extensive the collapse the greater the chance of developing cor pulmonale.

SUMMARY

Five patients with a thoracoplasty who developed cor pulmonale as a complication are reported with physiological studies. All five patients studied had typical findings, on intracardiac catheterization, of cor pulmonale.

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SOLITARY PULMONARY ADENOMA (FOCAL PULMONARY ADENOMATOSIS): A THREE-YEAR FOLLOW-UP AFTER RESECTION

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UNTIL recently, the diagnosis of pulmonary adenomatosis was made only at autopsy. However, an increasing awareness and interest in this entity has resulted in a number of instances of clinical diagnoses and, in a few, of treatment by surgical resection.

From 1896, when Livingood[1] described the multicentric nature of spontaneous lung tumors in mice, there has been controversy as to the origin of the tumors of pulmonary adenomatosis and of alveolar cell carcinomas of the lung. However, there has been fair agreement on the multicentric nature of these tumors. Delarue and Graham[2] emphasized this point and cautioned against false optimism following resection. They reported a case with an uneventful recovery following right lower lobe resection in June, 1943. The patient remained well until the fall of 1946, when he developed a productive cough, weight loss, and pain in the right chest and arm. In December, 1947, the remainder of the right lung was resected, but there had been invasion of local tissues so that, despite the fact that the left lung was still clear in September, 1948, the authors felt the prognosis was guarded.

More recently, Osserman and Neuhof[3] reported a five year follow-up without recurrence in a 44-year-old woman who had had a left lower lobe resection for localized "mucocellular papillary adenocarcinoma."

Both the case reported by Delarue and Graham[2] and that reported by Osserman and Neuhof[3] were symptomatic.

We believe the following case worthy of reporting because of the youth of the patient, the asymptomatic course, the long preoperative roentgenographic observation, and the lack of recurrence over the three-year postoperative period.

CASE REPORT

M. C., a 16-year-old applicant for a summer job at the Philadelphia Navy Yard, had a pre-employment 46 mm. photofluorogram on June 29, 1944 (Fig. 1), which revealed a small rounded mass with a central area of rarefaction at the left base. During this period in the survey work of the Philadelphia Tuberculosis and Health Association no routine follow-up was maintained, reliance having been placed in the follow-up by the plant physicians. In the spring of 1945, one of the authors, in taking over the survey project, came across the photofluorogram in a casual study of previous significant films. The young man had been rejected for employment because of the findings and the family had moved, so he could not be found until July, 1945, when roentgenogram revealed no change (Figs. 2 and 3). He was a

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tall, well-nourished lad, entirely without symptoms. He had been a five-letter athlete in high school during 1944 and 1945. He was hospitalized for study at Temple University Hospital in September, 1945. Bronchoscopic examination was negative. Bronchial secretions yielded no tubercle bacilli. Despite a negative first strength P.P.D. test, he was discharged with a tentative diagnosis of tuberculoma. He was followed by serial roentgenograms and, in September, 1947, an increase in the size of the lesion was noted (Fig. 4). He was re-admitted still asymptomatic. Physical examination was negative. Biopsy by needle aspiration

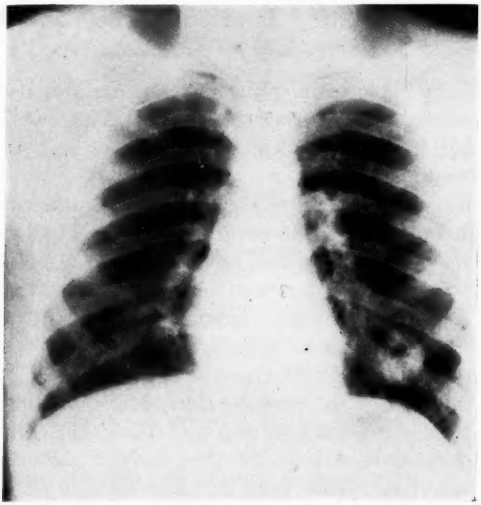

Fig. 1.—June 29, 1944. 70 mm. photofluorogram revealed rounded mass with central area of rarefaction at left base.

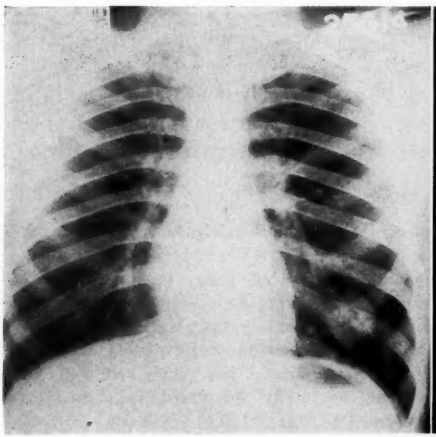

Fig. 2. Fig. 3.

Fig. 2.—July 11, 1945. 14 × 17 retake revealed no change.
Fig. 3.—July 11, 1945. Lateral reveals mass in left lower lobe.

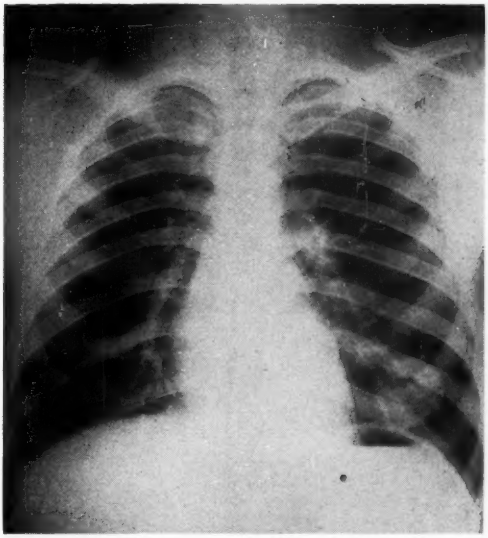

Fig. 4.—Sept. 15, 1947. Lesion has definitely increased in size.

Fig. 5.

Fig. 6.

Fig. 5.—Photomicrograph, low magnification, showing alveolar arrangement of tumor cells.

Fig. 6.—Photomicrograph, high magnification, showing mucin-secreting cells and their nonmalignant character.

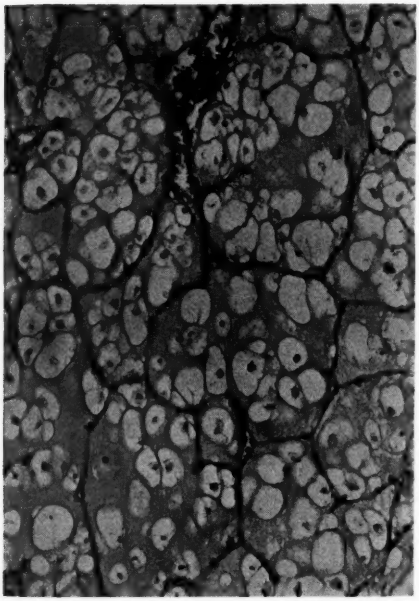

Fig. 7.—Photomicrograph of tumor, showing sloughing and disintegration of tumor cells to form sticky exudate.

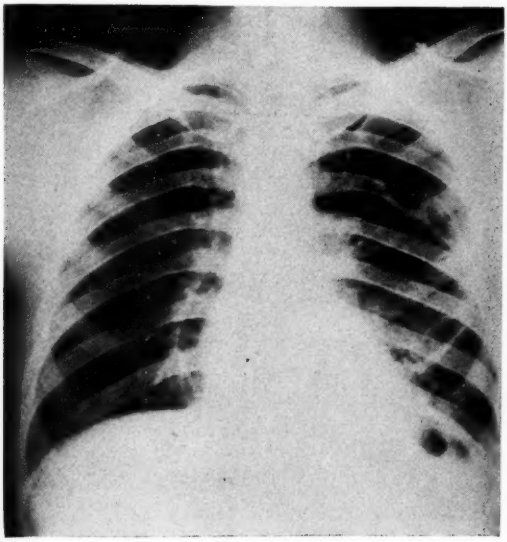

Fig. 8.—Aug. 1, 1950. No recurrence visible.

was noncontributory. Laboratory tests were normal except for a white cell count of 13,000 with 88 per cent neutrophilic leucocytes. At operation, Nov. 4, 1947, a tumor of approximately 7 cm. diameter was found in the left lower lobe, near the interlobar fissure directly beneath the pleura. The entire mass was removed with a margin of lung tissue for biopsy.

The surgical specimen was a flat piece of tissue covered on one surface by pleura measuring approximately 5 cm. in diameter. The specimen was about 3 cm. thick. In its substance there was a spheroid mass which was rather soft and had a pinkish color. It was in close proximity to the pleura along one surface; elsewhere it was poorly delineated, merging imperceptibly into normal lung tissue. When it was sectioned an astonishing quantity of clear, sticky exudate emerged. It had the appearance and consistency of rather thin egg white. The central portion of the mass was cystic, containing more of this clear exudate.

Blocks were fixed in formalin solution and sectioned. They presented a bizarre microscopic appearance. The entire mass was composed of alveolar structures which had the size and pattern of pulmonary alveoli without alveolar ducts (Fig. 5). The walls of these structures looked like alveolar partitions, and this resemblance was enhanced by the presence of several capillary blood channels. Most of the structures were lined by a single layer of tall, narrow, cylindrical cells measuring from 75 to 100 micra in length and 10 to 20 micra in width. The nuclei, about 10 micra in diameter, were uniform, darkly chromatinized and situated at the extreme bases of the cells. They lacked the appearance which is associated with a malignant behavior. The cytoplasm stained poorly and under high magnification was seen to consist of various sized globules of mucin. The cells were not ciliated. The alveolar lumen was filled with the same mucinous substance which formed the cytoplasm (Fig. 6). It was impossible to tell whether the free mucin was formed by secretion or by sloughing and disintegration of the alveolar lining cells, though there was a considerable amount of the latter leaving many of the alveolar partitions completely bare (Fig. 7).

The postoperative course was uneventful. Focal adenomatosis was the final diagnosis. No recurrence has been demonstrable (Fig. 8). It is noteworthy that no change occurred in this lesion until more than three years after it was first found.

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THE INFLUENCE OF STREPTOMYCIN RESISTANCE UPON THE SUCCESS OF CAVERNOSTOMY FOR THORACOPLASTY FAILURE*

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THE August, 1950, issue of THE JOURNAL OF THORACIC SURGERY contained a report[1] of a series of 23 thoracoplasty failures who were treated at the Veterans Administration Hospital, Oteen, North Carolina, with an Eloesser type cavernostomy. These patients were operated upon in late 1946 and early 1947. Streptomycin was not in common use at that time. Only two of the patients in the series had received the drug prior to the time when an attempt was made to close the cavernostomy sinus. A negative sputum and closure of cavity were obtained in 81.2 per cent of sixteen patients. Streptomycin was used as an adjunct at the time of closure of the residual sinus. The results impressed us so favorably that we subsequently chose the operation in place of resection in a number of instances.

As the therapeutic application of streptomycin in tuberculosis has become more widespread, we rarely receive patients for treatment who have not had one or more courses prior to consideration for surgery. The patients reported in the original study have continued to do well. The series has now been expanded to a total of forty-one patients. Twenty-five of these had received streptomycin prior to the open cavity drainage.

More than 3,000 articles have appeared in the literature since the discovery of streptomycin in 1944 by Schatz, Bugie, and Waksman,[2] and the report by Feldman and Hinshaw[3] concerning its activity against *M. tuberculosis.* Many of these have dealt with the application of the drug to the surgery of tuberculosis.

The protective action of streptomycin against spreads, bronchopleural fistula, and empyema following thoracic surgical procedures has been repeatedly emphasized. As early as 1948, however, evidence began to appear indicating that the unrestricted use of streptomycin in thoracic surgery was useless, and possibly harmful. At that time the Veterans Administration discontinued the routine use of streptomycin as a prophylactic agent during thoracoplasty for tuberculosis.

Since then, except in the several "Transactions of the Streptomycin Conferences" little has been written, concerning the effects of previous streptomycin treatment and the development of resistance upon the results of surgery for tuberculosis. During the Sixth Streptomycin Conference in 1948, Coleman and Bunch[4] asked the question, "Is Pulmonary Resection Safe in Patients Previously Treated with Streptomycin?" After citing two unfavorable cases, their con-

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clusion was to the contrary. Early in 1949, Murphy and Seiler[5] studied the question of bronchopleural fistulas following pulmonary resection in patients who had been treated with streptomycin prior to their resection course. An incidence of 25 per cent of fistula development was encountered in the previously treated patients, as compared with 5 per cent in those who had received no streptomycin previous to resection.

Later in 1949, Murphy, Seiler, and Walkup[6] discussed complications following resections in patients previously treated with streptomycin. They tabulated the incidence of spreads, bronchopleural fistulas, late reactivation, empyema, wound infection, and the mortality rate, and found that in each case the rate was higher in the previously treated than in the untreated patients.

The following year, 1950, Murphy and Walkup[7] again stated that the incidence of complications was higher in a streptomycin resistant group than in a nonresistant group of previously reported patients who had been given a thoracoplasty for tuberculosis. The work included the results after resections or cavernostomies in the thoracoplasty failures.

The "Quarterly Progress Reports of the Veterans Administration Streptomycin Committees"[8] in July, 1950, reviewed the statistics of the surgical staff of the Veterans Administration Hospital, in Minneapolis, Minn. Results after sixty-four resections performed at the Minneapolis Hospital were compared with those after 630 resections performed in other Veterans Administration Hospitals. It was found that in a group of 408 lobectomies there were marked differences in the rate of sputum conversion and incidence of postoperative complications between streptomycin resistant and previously nontreated groups. Fifty per cent higher incidence of sputum conversion was found in the previously untreated group. They found three times as many postoperative spreads, fifteen times greater incidence of bronchopleural fistulas, and twenty-five times greater incidence of empyema in the resistant group. There were comparable figures in the pneumonectomy group. In the sixty-four resections performed at their own hospital, similar results were obtained.

The earlier studies quoted have given considerable evidence as to the harmful effects of streptomycin resistance upon the results of excisional surgery and thoracoplasty for tuberculosis. Since our recent results following cavernostomy for thoracoplasty failure have been discouraging, we decided to analyze the series and attempt to determine if streptomycin resistance was a factor.

This paper compares the results following cavernostomy in patients who have not had previous streptomycin treatment with those who have had such treatment.

The indications for operation and the operative technique as given by Murphy and Koontz in their original description have been constant throughout the entire series.

Table I demonstrates the influence of streptomycin on cavity closure.

Cavities Opened.—Forty-one cavities in an equal number of patients have been opened by an Eloesser type cavernostomy. Sixteen of these patients had not received streptomycin therapy previously. Twenty-five patients had been previously treated with streptomycin, and twenty-three of these were known to be resistant.

TABLE I. INFLUENCE OF STREPTOMYCIN ON CAVITY CLOSURE

	CAVITIES OPENED	CAVITIES CLOSED		PER CENT CLOSURE	AVERAGE IN WEEKS OF DRAINAGE
		PRIMARY	SECONDARY		
Without Previous Streptomycin	16	8	5	81.2	18.6
With Previous Streptomycin	25	3	4	28.0	31.3

Cavities Closed.—Thirteen of the sixteen patients who had not received previous streptomycin therapy, or 81.2 per cent, obtained a successful eradication of the cavity by cavernostomy alone. Eight of these healed primarily following surgical closure and five healed secondarily, exhibiting cutaneous fistulas for varying lengths of time. Of the three patients classified as cavernostomy failures, two eventually underwent resection. One of these failures died (to be discussed later). A negative sputum was obtained in both of the patients who had a resection. One of these developed a postoperative bronchopleural fistula. Only 7, or 28.0 per cent, of the 25 patients who had been previously treated with streptomycin could be classified as successful cavernostomies. Three of these healed primarily following surgical closure, and four healed secondarily. Ten of the remaining eighteen patients have persistent cavities.

An attempt at surgical closure failed in eight patients. Ten never fulfilled the criteria for surgical closure. Resection was performed in five patients in whom surgical closure was unsuccessful. Three of these healed and a negative sputum was obtained. Two of the resection patients died.

Average Duration of Drainage, in Weeks.—This column in Table I denotes the number of weeks elapsing from the time the cavity was opened until it was felt that surgical closure of the wound was feasible. Closure was attempted when the cavity was no longer visible on planigraphic roentgenographic studies, and no longer palpable on digital examination through the cavity stoma. In most instances, also, the tract was epithelized and the drainage reduced to a scanty mucoid material. Smears and cultures of the sinus drainage were usually found to be negative for acid-fast bacilli. The figure of 18.6 weeks represents the average drainage time of the thirteen successful cavernostomies performed in patients who had not been previously treated with streptomycin. The longest drainage time in this group was twenty-eight weeks, and the shortest six weeks.

The average drainage time of the seven successful cavernostomies performed in the group who had previously been treated with streptomycin was 31.3 weeks. The longest time was thirty-six weeks, and the shortest 20 weeks. It is of interest to note that the shortest drainage time in the previously treated group was longer than the average drainage time for the previously untreated group. The ten previously treated patients, having persistent cavities, have continued to drain an average of 50.4 weeks.

Table II demonstrates the influence of streptomycin on sputum conversion and complications.

Prior Positive Sputum.—Fifteen of the sixteen previously untreated cases had a postive sputum prior to the time of cavernostomy. Twenty-three of the twenty-five previously treated cases had positive sputum preoperatively.

TABLE II. INFLUENCE OF STREPTOMYCIN ON SPUTUM CONVERSION AND COMPLICATIONS

	PRIOR POSITIVE SPUTUM	SPUTUM CONVERSION		SPREADS		WOUND INFECTIONS		DEATHS	
		NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	EARLY	LATE
Without Previous Streptomycin	15	13	86.6	1	6.2	1	6.2	1	0
With Previous Streptomycin	23	10	43.5	9	36.0	4	16.0	2	3

Sputum Conversion.—Thirteen of the fifteen previously untreated patients who had preoperative positive sputum, or 86.6 per cent, obtained a sputum negative by culture. Only ten of the twenty-three previously treated cases with positive sputum, or 43.5 per cent, obtained a conversion of sputum. The patients with no prior treatment showed approximately 50 per cent greater incidence of sputum conversion.

Spreads.—In the group of sixteen streptomycin "virgins" undergoing cavernostomy, there was a contralateral spread in the patient who developed traumatic pneumothorax and died on the eleventh postoperative day. Among the group of twenty-five previously treated patients there were nine spreads, a total of 36.0 per cent.

Wound Infections.—The question of wound infection is hard to evaluate in cavernostomies, since all of the wounds, due to the nature of the operation, show some degree of infection. In this series only those patients in whom there was a definite wound breakdown or progression of the infection beyond the operative area were classified as having an infection. In the group that had been previously treated with streptomycin there were four, or 16.0 per cent, who showed a definite wound infection.

Deaths.—In the group not receiving previous streptomycin, there was one early death. This occurred eleven days following the second stage, at which time a traumatic pneumothorax was incurred. In the previously treated group there were two early and three late deaths. One of the late deaths occurred after discharge from the hospital, and the other two followed resection for cavernostomy failure. One of the early deaths followed the opening of the cavity, at which time a spinal foramen was entered during the course of needle exploration. Tuberculous meningitis resulted. The other early death resulted from a massive bilateral caseous spread following the cavernostomy closure.

CONCLUSIONS

1. A study of forty-one consecutive cases undergoing cavernostomy for post-thoracoplasty residual cavity reveals that: (a) Sixteen of these had not received streptomycin prior to the surgery, and twenty-five had been previously treated with streptomycin. Twenty-three were resistant to over 10 micrograms per milliliter prior to cavernostomy closure. (b) The operation was more satisfactory and the incidence of sputum conversion was much higher in the previously untreated patients. (c) The incidence of complications was much higher in patients with resistant bacilli than in those who had received no streptomycin prior to closure of their cavities.

2. The indiscriminate use of streptomycin in the treatment of tuberculosis should be condemned.

3. A cooperative medical and surgical study of each candidate should be made prior to initiation of therapy so that the beneficial effects of streptomycin could be given the patient when his needs are most urgent.

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